A CLINICAL STUDY OF HEMANGIOMAS AND VASCULAR MALFORMATIONS

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CERTIFICATE

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INTRODUCTION

A hemangioma is an abnormal proliferation of blood vessels that may occur in any vascularized tissue. Considerable debate exists as to whether these lesions are neoplasms, hamartomas, or vascular malformations. Mulliken strongly supports classification of hemangiomas as neoplasms[1], whereas Godanich and Capanacci[2] seem to favor a hamartomatous classification. There seems to be consensus that the term "hemangioma" should refer to "hemangiomas of infancy," which have a predictable natural history that includes absence at birth followed by a period of growth over 6-18 months and then a period of involution that may take several years[3].

Vascular malformations have been recognized throughout history as birthmarks. The cause was thought to be maternal cravings for fruit or maternal dreams, moods, and fantasies. Although Blondel disproved these theories in 1727, some persist today. In 1866, Dugas conducted a scientific analysis of birthmarks and concluded that they were caused by defects in embryonic development. Virchow and Wagner established the first classification system of vascular malformations, based on channel architecture and histomorphologic appearance.

REVIEW OF LITERATURE

In 1982[1], Mulliken and Glowacki proposed a classification system for vascular birthmarks that correlated natural history and physical examination with clinical features; which were subsequently accepted by the International Society of Vascular Anomalies in 1996[4]. On the basis of cellular kinetics and clinical behavior, there are two major categories of vascular anomalies:

1. Tumors – lesions that arise by endothelial hyperplasia

2. Malformations – lesions that arise by dysmorphogenesis and exhibit normal endothelial turnover.

Tumors	**Malformations**
Infantile hemangioma	Capillary
Congenital hemangioma	Venous
Verrucous hemangioma	Arterial (AVM, AVF, Ectasia, aneurysm)
Hemangioendothelioma	Lymphatic
Miliary hemangiomatosis of infancy	Mixed
Tufted angioma, Glomangioma	

	Tumors	**Malformations**
Present at birth	Usually postnatal, rarely fully grown at birth	Usually at birth
Male: female ratio	1:3-1:5	1:1
Incidence	1-2.6% at birth, 10-12% at 1 year	0.3-0.5%(portwine stain)
Natural history	Phases: proliferating, involuting, and involuted	Proportionate growth can expand
Cellular	Endothelial hyperplasia	Normal endothelial turnover
Skeletal changes	Occasional mass effect on adjacent bone; rare hypertrophy	Slow flow: distortion, hypertrophy, or hypoplasia Fast flow: destruction, distortion, or hypertrophy

Modified from Mulliken and Young[5]

VASCULAR TUMORS

INFANTILE HEMANGIOMA

DEFINITION:

It is a benign vascular tumor that appear during first months of life, and which characteristically have an initial proliferative phase, followed by involuting phase and ending with an involuted phase[6].

ETIOPATHOGENESIS:

Hemangiomas are benign tumors that exhibit an early and rapid proliferative phase during the first year of life characterized by endothelial and pericytic hyperplasia, followed by a slower but steady involution phase that may last for years. Neither the cause nor the cell of origin of infantile hemangiomas has been elucidated. Theories abound and several lines of evidence support several divergent theories of the cell of origin, including placental tissue, endothelial progenitor cells, and mesenchymal stem cells.

Cheung and colleagues[7] compared the concordance of hemangioma in monozygotic versus dizygotic twins and found no evidence of a strong predisposing inherited component. However, Blei and colleagues described six rare families segregating hemangiomas and/or vascular malformations as an autosomal dominant trait with incomplete penetrance[8]. This suggested a predisposing mutation in these families

segregating the trait. Genetic involvement was bolstered with the genetic mapping of a locus on chromosome 5q for hemangioma/malformation development in these particular families[9], but the gene responsible has yet to be identified.

Boye and colleagues[10]showed that endothelial cells derived from hemangioma are clonal in origin and demonstrating that they arise from a common precursor cell. Mesenchymal stem cells may also play a role in the formation of infantile hemangiomas. These cells have been identified in hemangioma tissue. Mesenchymal stem cells retain the capacity to differentiate into numerous mesodermal cells, including adipocytes, suggesting that these cells may be the source of the resultant adipose tissue found in involuted hemangiomas[11].

It has also been suggested that there may be analogies with retrolental fibrovascular proliferation seen in premature infants given oxygen therapy, and this concept receives an indirect support from the higher incidence of infantile hemangiomas in infants born prematurely[12]. An imbalance has been demonstrated between expression of angiogenic and anti-angiogenic factors within infantile hemangiomas and adjacent normal tissue. Endogenous steroid hormones also play a role in the growth of infantile hemangiomas. Both increased serum levels of 17 βestradiol and increased number of tissue receptors for this hormone in the proliferating infantile hemangioma has been demonstrated[13].

An alternative interpretation of the present data comes from work of North and colleagues, who have documented the expression of placental vascular epitopes in hemangiomas. Hemangiomas display high levels of immunostaining for the GLUT1 glucose transporter [14], a surface protein that is highly expressed in most of the embryonic and fetal endothelial cells but is lost in most tissues except at the blood-tissue barriers, including microvessels in the central nervous system and the placenta. North et al. have expanded on this initial finding to show that other antigens associated with placental vessels, including FcγRII, Lewis Y antigen, and merosin, are also expressed in hemangioma[15].

The similarities in gene expression between hemangioma and placental vessels might be explained by a somatic mutation in a regulatory gene that directs hemangiomal endothelial cells toward a placental phenotype, but North and colleagues also suggest an alternative theory. Embolic placental endothelial cells could reach fetal tissues from chorionic villi through right-to-left shunts characteristic of the normal fetal circulation. If the embolus contained a single endothelial cell or only a small number of endothelial cells, this would also be compatible with the clonality results obtained by Boye and colleagues[10]. The fact that chorionic villus sampling increases the risk of hemangiomas further supports this model, since the local placental injury caused in this procedure might increase the shedding of endothelial cells from chorionic villi into the fetal circulation[16,17].

The placenta and hemangioma share a similar life cycle of robust vascular growth. The placenta produces very high levels of the proangiogenic cytokine, vascular endothelial growth factor (VEGF). As a protective mechanism against uncontrolled angiogenesis in the fetus and mother, a soluble form of the VEGF receptor, sFlt-1, found in both amniotic fluid and maternal serum, is also produced by the placenta. sFlt-1 binds circulating VEGF, preventing excessive angiogenesis in nonplacental tissues. During postpartum, the connection to the placenta and sFlt-1 is removed, abrogating this negative feedback and allowing proliferation of cells, such as those in hemangiomas, responsive to VEGF[18,19].

Several VEGF receptors (VEGFRs) may play a role in the development of hemangiomas. VEGFR1 on endothelial cells acts as a decoy receptor such that the binding of VEGF to this receptor does not effect a change in the endothelial cell. However, the binding of VEGF to VEGFR2 elicits endothelial cell proliferation and migration. Hemangioma endothelial cells exhibit low levels of VEGFR1, with marked constitutive activation of VEGFR2. Gene transcription for VEGFR1 in hemangioma cells is dependent on nuclear factor of activated T cells (NFAT). This, in turn, is dependent on a pathway involving beta1 integrin, VEGFR2, and integrin like receptor tumor endothelial marker-8.

Missense mutations in genes encoding for VEGFR2 and tumor endothelial marker-8 have been identified in a subset of infantile hemangiomas. These mutations are likely to be responsible for the constitutive activation of VEGFR2 and resultant endothelial cell proliferation. Soluble VEGFR1 or anti-VEGF antibodies normalize the constitutive VEGFR2 signaling[20].

PATHOLOGY:

Proliferative phase:

In the earliest phase of growth of infantile hemangiomas, there is a solid mass of proliferating endothelial cells, with few if any lumina. Later in the proliferative phase, capillary sized lumina are apparent, lined by plump endothelial cells. Endothelial cells express phenotypic markers of maturity such as CD 31, factor VIII related antigen (von willebrand factor). Reticulin staining confirms that each group of endothelial cell is surrounded by a limiting membrane of reticulin fibres. PAS staining shows thickened basement membrane beneath the endothelial cells lining the lumina. Immunohistochemical studies have documented increased expression of basic fibroblast growth factors[21]. Increase in vascular endothelial growth factor / vascular permeability factor has also been documented. The mast cells help in endothelial proliferation and are found in high numbers in proliferating hemangiomas[22].

Involuting phase:

Regression is characterized by dilatation of vascular lumina, flattening of the endothelial cells and progressive deposition of perivascular fibrous tissue, which establishes a lobular architecture. Inhibition of matrix metalloproteinase, a protein that suppresses formation of new blood vessels also occurs during the involuting phase[23].

Involuted phase:

After regression is complete, all that remains are a few tiny, capillary like feeding vessels and draining veins, lined by flat, mature endothelium and surrounded by islands of loose fibrofatty tissue intermingled with dense collagen and reticular fibers[23].

CLINICAL FEATURES:

Infantile hemangiomas are the commonest tumors of infancy, with a prevalence of about 4%-10% of full term white neonates; more often in girls (ratio 3:1 to 5:1) [24]. They are less common in infants of African or Asian descent. There is a higher incidence in infants born prematurely; about 13% at 1 year for all preterm infants, increasing in inverse relationship to birth weight[5]. At 1 year, the prevalence in preterm babies with a birth weight below 1500g is about 16%, and, in preterm babies with a birth weight below 1000g, about 23%. Conversely, the prevalence in preterm babies with a birth weight over 1500g is no different from that

of full-term babies. The prevalence of infantile hemangiomas at 1 year in preterm infants was shown to be inversely related to gestational age at birth, being recorded as 8% for babies born after the 35th week, 11% for those born between the 30th and 35th weeks, and 19% for those born between the 25th and 29th weeks[25].

Infantile hemangiomas become apparent during the first month of life in about 90% of cases, and virtually 100% by the ninth month. Approximately 65% of infantile hemangiomas are superficial, 15% deep and 20% mixed[6]. Hemangiomas typically are single tumors, but 20% grow in multiple cutaneous sites, including other organ systems, notably liver, gastrointestinal tract, brain etc. Approximately 30%-50% of hemangiomas are nascent at birth, presenting as a barely visible pale spot, a telengiectatic/ macular red stain, or as a pseudoecchymotic patch. The term congenital hemangioma defines a tumor that is fully developed at birth and does not exhibit the usual postnatal rapid growth[23].

Proliferating phase:

The superficial infantile hemangioma is most commonly known as a strawberry nevus or strawberry hemangioma, on account of its usual clinical appearance in the form of a sharply circumscribed oval or round, soft, domed swelling of intense scarlet-red color as it permeates the superficial dermis. The surface may be smooth or lobulated. It is firm,

tense, and non-compressible. These lesions may occur at any site, but about 60% occur on the head and neck followed by trunk in 25%[6].

If tumor spreads within the lower dermis, subcutis or muscle, however the overlying skin is only slightly raised, warm, and bluish in color. Draining veins are commonly seen radiating from the tumor. Hence there is frequently a deep element to superficial infantile hemangiomas of strawberry type, particularly when these are large; such lesions should be termed mixed infantile hemangiomas. Deep infantile hemangiomas often feel like a 'bag of worms', and a useful feature in their distinction from other tumors is that they can generally be compressed to about half their original size, quickly regaining their original dimensions on release of pressure. Similarly, they often become larger and darker when the child screams or cries[6].

The growth of infantile hemangiomas typically begins to stabilize by 10 to 12 months. Spontaneous epithelial breakdown, crusting, ulceration, and necrosis complicate 5% of cutaneous hemangiomas[26]. Ulceration is less common than bleeding, although it is particularly likely to complicate lesions in the anogenital area, where it may result in dysuria or pain on defecation. Ulceration similarly tends to complicate lesions at other sites which are vulnerable to trauma, such as the ears, nose or the lips[23].

Involuting phase:

Usually after 1 year, hemangiomas seem to grow in proportion to the child and then clinical signs of regression appear. Resolution of superficial infantile hemangiomas is heralded by softening of the lesion and by the appearance of opaque, pinkish grey areas in the centre of the surface. These foci gradually become confluent and extend towards the periphery of the lesion[6].

Virtually 100% of infantile hemangiomas undergo spontaneous regression, which is complete or almost complete in about 95%. About 30% of infantile hemangiomas lesions will have resolved by the fourth year, about 50% by the fifth and 75% by the seventh, gradual improvement continues till age 12[27]. The likelihood of early resolution is not affected by the size of the lesion, its site, or by the number of lesions present.

Involuted phase:

Nearly normal skin is restored in approximately 50% of children. Stigmata of involuted infantile hemangioma include telengiectasias, and at certain sites, particularly the lips and eyelids, it is common for there to be a residual sac of redundant and slightly atrophic skin[23]. An early onset of resolution is generally associated with a more rapid disappearance and a superior cosmetic result. Conversely, a late start to resolution is generally associated with a higher chance of incomplete regression. Areas

of previous ulceration frequently leave yellowish scars. Lesions in the scalp usually resolve without permanent alopecia in the affected area, unless previous ulceration has occurred. Perhaps the commonest lesions that fail to show complete resolution are lesions on the nose, ears and lips[6].

COMPLICATIONS:

Ulceration: [28]

Ulceration is frequently complicated by infection, and when it occurs on the ears, nose or lips, permanent loss of tissue and mutilation may result, sometimes very rapidly. Recurrent bleeding may also complicate ulceration. Ulceration is likely to be followed by scarring.

Haemorrhage:

Only rarely is bleeding from an infantile hemangioma substantial, except in the Kasabach-Merritt syndrome or during surgery. Normally, compression will stop bleeding[6].

Infection:

Secondary infection may complicate infantile hemangiomas in the event of ulceration or following any type of surgical interference. Occasionally, this may lead to septicaemia, with a potentially disastrous

outcome. Group A streptococci appear to be particularly dangerous in this situation[6].

Malignant change:

Although malignant change may be a complication of hepatic hemangiomas, it never complicates cutaneous infantile hemangiomas. However, true malignant vascular tumours in infants might conceivably be initially mistaken for infantile hemangiomas, particularly when they have a deep location. Such tumours include malignant hemangioendotheliomas[29] and malignant hemangiopericytomas30.

Systemic hemangioma:

Visceral infantile hemangiomas may occur with or without coexistent cutaneous infantile hemangiomas. It may be found in liver, GIT, lung, spleen, pancreas, heart, kidneys, adrenals, bladder, brain etc. High-output cardiac failure is the commonest cause of death, and this is most often induced by arteriovenous shunting in the liver or lungs. Other complications included are the Kasabach-Merritt syndrome, convulsions, and obstructive jaundice[6].

Heart failure:

Shunting of large volumes of blood through infantile hemangioma may lead to high-output heart failure. This complication is particularly

likely to occur in association with multiple infantile hemangiomas, when it is usually due to shunting through one or more hepatic hemangiomas[31].

Kasabach meritt syndrome:

It is characterized by thrombocytopenia (due to platelet trapping), coagulopathy, and microangiopathic hemolytic anemia in association with a rapidly enlarging vascular lesion. It was traditionally felt to be a complication of infantile hemangiomas, but is now associated with different vascular tumors, namely kaposiform hemangioendothelioma[32] and tufted angioma[33].

Infantile hemangiomas leading to the Kasabach-Merritt syndrome are generally single deep lesions of larger size, but the disorder can very occasionally occur in association with smaller and more superficial lesions. The responsible infantile hemangioma will most commonly occur on the trunk, neck and proximal parts of the limbs, particularly the thighs and shoulders and, relatively uncommonly, on the head. The coagulation defect almost always becomes apparent during the first few weeks of life, but may already be apparent at birth. The onset of defective coagulation is most commonly heralded by bleeding into and around the angioma or manifested by an increase in size, induration, tenderness and superficial ecchymoses. The resulting rapid expansion of the angioma may cause potentially lethal compression of neighbouring vital structures, particularly when the lesion is in the cervicofacial area[6].

In addition to thrombocytopenia other laboratory findings include anemia, hypofibrinogenemia, elevated D-dimers, fragmentation of erythrocytes on manual smear, and prolonged coagulation studies. The mortality rate is high, from 10-30%[34].

Impairment of vision:

Infantile hemangiomas involving the eyelids can interfere with vision in several ways. Firstly, obstructive amblyopia may result if the lesion directly obscures the line of vision. Secondly, such lesions may also lead to astigmatism, even when the line of vision is not obstructed, probably due to a direct pressure effect on the cornea; this can lead to astigmatic amblyopia[35].

Airway obstruction:

It is important to consider the possibility that any infant with a cutaneous hemangioma may concurrently have a subglottic hemangioma. This is most likely if the cutaneous lesion is in the neck, from which there may be direct extension into the subglottic airway. Such an event may require an emergency tracheotomy for its relief. Involvement of the nose in the neonatal period may also obstruct respiration, as neonates normally will not breathe through the mouth[36].

Interference with feeding:

Feeding difficulties may complicate hemangiomas in the mouth and those that obstruct nasal breathing[6].

Obstruction of external auditory canal:

Hemangiomas that encroach on the ear may obstruct the external auditory canal. Although this will interfere with hearing in the short term, it will generally not affect the development of normal ear function in the longer term. Bilateral obstruction after the age of about 1 year would, however, be likely to interfere with normal speech development, but must be very rare[6].

Deformation of bone:

Minor deformities of bone occasionally results from direct pressure of an angioma, on the calvarium for example. Very rarely, large infantile hemangiomas of the face may provoke overgrowth of the facial skeleton or of the auricular cartilage[6].

Other associations:[37]

PHACES is one of the major associations. It includes Posterior fossa anomalies, Hemangioma, Arterial anomalies, Coarctation of aorta, Eye abnormalities, Spinal dysraphism and supra umbilical raphe.

DIAGNOSIS:

1. **By clinical presentation** → Hemangioma is non-blanching; firm to rubbery on palpation.

2. **Biopsy:**

In the earliest phase of growth of infantile hemangiomas, there is a solid mass of proliferating endothelial cells, with few if any lumina. The nuclei are not pleiomorphic, and only occasional mitoses are visible. Later in the proliferative phase, capillary-sized lumina are apparent, lined by plump endothelial cells. Reticulin staining confirms that each group of endothelial cells is surrounded by a limiting membrane of reticulin fibres. Periodic acid-Schiff (PAS) staining shows a thickened basement membrane beneath the endothelial cells lining the lumina. Initially, these lumina are slit-like, but gradually they become more dilated. Mast cells are plentiful during the proliferative phase[22].

The hemangioma becomes progressively more organized, with distinct lobules separated by fibrous septa containing the larger feeding and draining vessels. In older lesions the number of vascular channels decreases, and the diameter of the lumina increases with flattening of the endothelial lining, resulting in a 'cavernous' appearance, which must not be confused with the appearance of a venous malformation. There is a simultaneous progressive increase in intra- and interlobular connective tissue and fat[23].

3. Ultrasonography with colour flow imaging:[38]

It is useful in differentiating deep hemangioma from vascular malformations. The sonographic hallmark of proliferating phase hemangioma are dense parenchyma and fast flow. Hemangioma shows decreased arterial resistance, increased venous velocity on duplex evaluation and discrete soft tissue mass effect with conventional ultrasonography.

4. MRI :[39]

It is the "gold standard" for evaluation of a vascular anomaly; however it generally requires sedation or general anaesthesia if child is less than 6 years of age. Hemangioma appears as a parenchymatous tissue of intermediate intensity on T1-weighted, spin- echo images and moderate hypertintensity on T2- weighted, spin echo images. Exact localization, extent of involvement and with midline lesions, Presence of associated cranial / spinal dysraphism can be readily identified.

5. CT

6. Placental markers:High Endothelial immunoreactivity for erythrocyte type GLUT 1, merosin1, Lewis Y antigen (LeY) and fc (γ) R II[6].

TREATMENT:

In the absence of complications or where there is substantial cosmetic handicap, the correct management of infantile hemangiomas is generally expectant. No treatment is indicated where a good cosmetic result can be predicted[34].

Following are the considerations for evaluation, referral, and /or therapy[34]:

- Life threatening
- Interfering with vital functions

  Periocular

  Nasal tip

  Ear (extensive)

  Lips

  Genitalia, perineum

  Airway

  Hepatic

- Large facial
  "Beard" distribution
- Ulcerating
- Multiple

Treatment options include: (i) systemic corticosteroids; (ii) intralesional corticosteroids; (iii) topical corticosteroids under occlusion; (iv) laser therapy; (v) compression; (vi) surgical excision; (vii) embolization; (viii) vincristine; (ix) cryotherapy; (x) interferon (xi) sclerosant injection; and (xii) radiotherapy.

Treatment of ulceration or bleeding:

Ulcerated hemangioma is treated with daily cleansing, application of hydrated petrolatum, a topical antibiotic, or a hydrocolloid dressing and viscous lidocaine. Superficial ulceration usually heals within days to weeks; a deep ulceration can take longer. Flashlamp pulsed- dye laser is reported to aid healing and alleviate pain associated with ulcerated lesions[40].

Complete resection may be the most expeditious treatment, usually indicated for tumor located in scalp, chest, or extremity, but rarely for a facial lesion. If does bleeding occur, parents should be instructed to compress the bleeding area with a clean pad, holding pressure for exactly 10 minutes. Local tamponade controls bleeding in most circumstances; occasionally a suture is needed to control a bleeding site[23].

Corticosteroids:

Oral and intralesional corticosteroids are effective at slowing the growth and decreasing the size of proliferating infantile hemangiomas.

The mechanism of action has not been elucidated completely; however, corticosteroids appear to act by potentiating vasoconstrictive effects of epinephrine and norepinephrine on vascular smooth muscle. Evidence indicates that corticosteroids block estradiol receptors in hemangiomas in vitro. Response vary widely, from less than 40% to greater than 90%, depending on dose, duration of treatment, and age at which corticosteroid therapy is initiated[41]. Corticosteroid therapy should be administered during the proliferative phase because it has a negligible effect on involuting and otherwise stable infantile hemangiomas. The oral route generally is preferred over intralesional therapy; however, the location, size, patient age, and physician experience factor into the decision-making process. Prednisolone is initially given at 2to 3 mg/kg/day[23].

Intralesional corticosteroid should be considered for a small, well-localized cutaneous hemangioma and typically for lesions located in the nasal tip, cheek, lip, or eyelid. The goal is to minimize the volume of the proliferating tumor. Triamcinolone (2 to 3 mg/kg) is injected slowly at low pressure. On average, three sessions are needed at 6-8 week intervals. It has been suggested that potent topical steroids under occlusion may be an effective treatment approach for certain infantile hemangiomas[23].

Laser therapy:

Laser surgery is beneficial in treating both proliferating and residual vessels from hemangiomas. The flashlamp-pumped pulsed-dye

laser has become the most widely used laser for selective ablation of vascular tissue in childhood. Pulsed-dye laser surgery is effective for treating ulcerated hemangiomas and thin superficial hemangiomas, especially those on areas likely to result in significant functional or psychological impact (eg, fingers, eyes, lips, nasal tip, ears, face) [42]. Many ulcerated hemangiomas respond with decreased pain (sometimes as early as a few days after the initial treatment), rapid reepithelialization, and hastened involution.

Treatments generally are performed every 2-4 weeks until complete healing results. Occasionally, particularly with deep or combined superficial and deep lesions, ulceration may worsen with pulsed-dye laser treatment[43].

The risk of scarring or residual skin changes associated with pulsed-dye laser surgery of hemangiomas may be greater than without early laser treatment or with the treatment of capillary malformations, but the benefits of early involution should be weighed against the risks of a passive approach or alternative therapies. Other lasers that appear to be efficacious in treating hemangiomas include the pulsed Nd:YAG, frequency-doubled Nd:YAG. Carbon dioxide lasers are occasionally used for airway hemangiomas[44].

Surgical therapy:

The following are the indications for excision of infantile hemangiomas:

- Ulceration or repeated bleeding
- Redundant folds of atrophic skin
- For eyelid lesions that have not responded adequately to oral or intralesional corticosteroids
- At specific sites- for example at nasal tip[45].

Beta-adrenergic blocker: [46,47]

Beta-blockers, most specifically propranolol, have been recently used for infants with severe or disfiguring hemangiomas. Most infants reported have been treated with propranolol at a dose of 2-3 mg/kg/d in 2-3 divided doses. Duration of therapy varies from 2-10 months. As early as 24 hours after the initiation of therapy, many infantile hemangiomas have begun to change from intense red to purple, with evidence of softening. Most continue to improve until nearly flat and with significantly diminished color.

The mechanism of action is unknown; however, some hypothesize that local vasoconstriction may be a factor, which is based on the early color change and softening of the lesion. One study has demonstrated that nonspecific and beta2-selective blockers (eg,

propranolol) triggered apoptosis of capillary endothelial cells in adult rat lung tissue, suggesting a similar mechanism may be plausible for hemangioma endothelial cells.

Interferon alfa-2a or Interferon alfa-2b:[48,49]

Recombinant interferon should be considered the second line drug for endangering or life threatening hemangioma. Indications for IFN therapy include failure of response to corticosteroid, contraindication to prolonged systemic steroids, complications of steroid and rare instance of parental refusal to use corticosteroids.

The empirical dose of IFN is 2 to 3 million U/m^2, injected subcutaneously every day for 6 to 12 months. Side effects of IFN include elevated hepatic enzymes, transient neutropenia, and anemia. The most serious toxicity of IFN is spastic diplegia, which occurs in an estimated 5% of cases.

Biologic immune response modifiers: [50,51]

Topical Imiquimod cream is the only medication in this new class. It works by stimulation of toll-like receptor 7 (TLR-7) and increases local interferon alpha and gamma, through which it may exert antiangiogenic effects. In a mouse model, imiquimod-treated vascular tumors showed decreased tumor cell proliferation, increased tumor apoptosis, and increased expression of tissue inhibitor of matrix metalloproteinase-1,

with decreased activity of matrix metalloproteinase-9, both of which are observed in the natural involution of infantile hemangiomas. The other modalities include sclerotherapy, vincristine, embolic therapy etc.

CONGENITAL HEMANGIOMAS:

These are unusual tumors that have no female predominance and are fully grown in utero and do not have a postnatal growth phase. They differ from infantile hemangioma by their clinical features, pathology and their negative immunophenotyping for the placental markers[52]. They are further categorized into 2 types namely RICH and NICH.

Rapidly Involuting Congenital Hemangioma (RICH):

RICH appears as large, round or oval, bulging tumor, usually with a smooth surface and more often located on a limb close to a joint, on the forehead, cheek, scalp. Prominent telengiectasias are often seen on the surface, centre of the lesion is either nodular or necrotic and the mass is encircled by a white ring or halo. Spontaneous regression occurs within 6-14 months[53].

RICH are detected during prenatal ultrasound during third trimester and sometimes even as early as 16th week of gestation. It appears as an exophytic, hypoechoic mass traversed by multiple compressible channels with a predominantly venous flow[54]. Antenatal MRI is recommended to define the better characteristics of the vascular tumor. The pathologic

features of a RICH include large and small lobules of vessels embedded in fibrosis, as well as extralobular vessels. Some vessels have moderately plump endothelium; endothelial cells are negative for GLUT-1[53].

Non-Involuting Congenital Hemangioma (NICH):

A NICH is less impressive at birth than a RICH. The tumor is usually flat, and round or oval in shape. The centre varies from pinkish with minor telengiectasia and the location is similar to those of RICH. After birth NICH is fast flow by Doppler evaluation. And it may reveal minor arteriovenous fistulas. The pathology of a NICH includes rather large lobules made of small capillaries lined by endothelial cells with hobnail nuclei. Lobules are separated by dense fibrous tissue. Endothelial cells lack reactivity for GLUT-1[55]. Unlike a RICH, a NICH never involutes.

VASCULAR MALFORMATIONS

Vascular malformations can be localized or diffuse errors of embryonic development. The classification of these anomalies is based on the type of abnormal vascular channels and flow characteristics. The term vasculogenesis refers to the processes by which mesodermally derived endothelial precursors align to form primitive blood vessels. The term angiogenesis refers to the formation of new vessels from pre-existing vessels. The various types of vascular malformations can be envisioned as faulty development at some stage of either vasculogenesis or angiogenesis[23]. Most vascular malformations are sporadic, but some are inheritable in a classic mendelian autosomal dominant pattern. Molecular studies suggest that vascular anomalies are caused by dysfunctional signaling processes that regulate proliferation, apoptosis, differentiation, maturation, and adhesion of vascular cells[56].

CAPILLARY MALFORMATIONS:

CMs are composed of dilated capillary to venule sized vessel in the superficial dermis. It includes salmon patch and portwine stain.

SALMON PATCH:

syn. Naevus simplex; erythema nuchae; unna's naevus; 'stork bite'; 'angel's kiss

Salmon patches' are extremely common anomalies, which have been observed in the neonatal period in about 20-60% of children of all races[57]. There is evidence of a definite genetic influence in their aetiology, and both nuchal and facial salmon patches seem to be inherited in an autosomal dominant manner[58]. Clinically, the lesions take the form of irregular, dull, pinkish red, macular areas, often featuring fine, linear telangiectasia. The nape of the neck is by far the most commonly affected site, but facial lesions, on the glabella, forehead, upper eyelids, tip of the nose or upper lip are also frequent. Those on the face fade rapidly, and most will have more or less disappeared within a year. Nuchal lesions tend to be much more persistent, and probably remain unchanged into adult life in at least 30% of cases[6].

PORTWINE STAIN:

Syn. Naevus Flammeus

PWS is a congenital capillary malformation that may occur as an isolated lesion or in association with a variety of syndromes. These lesions present as macular stains with a pink to dark red color. Although an early PWS may be indistinguishable from an infantile hemangioma,

these lesions are usually distinguished by their congenital presence and their static nature, without the rapid proliferation and thickening that characterizes hemangiomas during the first year of life[34].

Etiology:

Capillary malformations and other vascular malformations are the result of abnormal morphogenesis. They are characterized by ectatic papillary dermal capillaries[6]. These ectatic vessels are lined by flat, benign-appearing endothelial cells, similar to the vessels of normal skin, with similar staining characteristics for endothelial antigens, including fibronectin, von Willebrand factor, and collagenous basement membrane proteins. The endothelial cells also exhibit cell turnover similar to normal vessels, supported by a paucity of mitoses or an uptake of tritiated thymidine.

Evidence supports a neural role in both the development and progression of capillary malformations. Animal studies show that the sympathetic nervous system influences the composition and functional properties of the vessel wall during development[23].

Immunohistochemical studies of capillary malformations reveal a significantly decreased density of perivascular nervous tissue in lesional skin, suggesting that inadequate innervation may be responsible for decreased vascular tone and progressive vascular dilatation[59]. Confocal microscopic studies demonstrate an inverse correlation between nerve

density and blood vessel diameter and evidence that capillary malformations with the lowest nerve density exhibit the highest blood vessel density and the poorest response to laser intervention[60].

The potent endothelial cell mitogen vascular endothelial growth factor (VEGF)–A and its most active receptor VEGF-R2 expression are significantly increased in capillary malformation skin tissue compared with control skin[61]. This may suggest that VEGF and VEGF-R could contribute to the pathogenesis of capillary malformations by inducing vessel proliferation and/or vasodilatation. If this is indeed a pathogenic factor, antiangiogenic treatments using VEGF blocking agents may prove to be useful for capillary malformations. Tie2 and angiopoietin-1 are known regulators of vascular remodeling during angiogenesis, mutations of which have been demonstrated in familial venous malformations[62].

An inactivating mutation of *RASA1* on 5q has been detected in some kindreds with multiple, small, round-to-oval, pink capillary malformations. *RASA1* encodes a GTPase-activating protein, which negatively regulates Ras activity[63].

Occasionally, lesions that appear to be identical to congenital port-wine stains have made their initial appearance in adult life, and may have followed trauma, possibly as a result of damage to the microvascular nerve supply. Familial multiple telangiectatic naevi having the

appearance of small port-wine stains have been reported on several occasions[6].

Clinical features:

Port wine stains are almost always present since birth. The reported incidence in the newborn has been from 0.1 to 2%. They vary in colour from a fairly pale pink to a deep red or purple, and in size from a few millimetres to many centimetres in diameter. PWS may progressively darken over many years, and occasional lesions develop secondary proliferative vascular blebs on their surface (cobble stone appearance) [64]. They may also become thickened and later in life. Port wine stains are often, but not always, unilateral and the most common site of involvement is the face, although they may occur on any cutaneous surface. In the face, there can be enlargement of the affected lip and gingival, and usually the maxilla or the mandible. In the limb, it is associated with limb hypertrophy both in length and girth. Associated eye and brain abnormalities occur in 8-15% of patients with facial port-wine stains[65].

Port-wine stains are not infrequently associated with adjacent areas of naevus anaemicus, and it has been suggested that this phenomenon may be explained by somatic recombination[66].

Treatment:

PWS lesions show little tendency toward spontaneous improvement or involution, and traditional therapy was limited to the use of tinted "cover-up" cosmetics. Laser therapy has revolutionized the treatment of these lesions, most notably the flashlamp pumped tunable pulsed dye laser. Flashlamp-pumped pulsed-dye laser (PDL) surgery is the treatment of choice for capillary malformations. It uses selective photothermolysis with ultrashort pulses of monochromatic yellow light (585-600 nm), which are preferentially absorbed by oxyhemoglobin in the abnormally dilated superficial dermal blood vessels. Flashlamp-pumped PDL causes selective destruction of these superficial target blood vessels, inducing intravascular coagulation and rupture of some smaller vessels, which later become absorbed and replaced by collagen. The ultrashort laser pulses are shorter than the thermal relaxation time of the vessels, thereby limiting adjacent dermal and epidermal heating and preventing subsequent damage. PDL therapy is usually performed over several sessions, separated in time by 6-8weeks, and can be quite effective in lightening these lesions[67].

STURGE WEBER SYNDROME:

Syn. Encephalofacial Angiomatosis

It is a neuroectodermal syndrome characterized by a PWS in the distribution of the first (ophthalmic) branch of the trigeminal nerve (V1) in association with leptomeningeal angiomatosis (presenting usually with seizures) and glaucoma. There are rare reports of patients with classic brain and ophthalmic findings in the absence of facial PWS[65].

PWS may also have multidermatomal or more extensive cutaneous involvement. In most cases, neurological symptoms have their onset during the first 2 years of life, and their first appearance after the age of 6 years is unusual. Some patients with extensive leptomeningeal angiomatosis remain asymptomatic throughout life. Seizures are the most common CNS feature, and often have their onset during the first year of life. The seizures are difficult to control, and both early onset and increased seizures intensity are associated with future developmental and cognitive delay[34].

Ocular involvement occurs in around 60% of patients with SWS. Glaucoma is the most frequent ocular finding, and it may be present at any time between birth and the fourth decade. It may be unilateral or bilateral. Vascular malformations of the eye in patients with SWS may involve the conjunctiva, episclera, choroid, and retina. Other eye findings include nevus of ota, buphthalmos, and blindness[34].

The EEG shows suppression of cortical activity over the affected area which may or may not be associated with focal epileptiform spike discharges. Cortical calcifications can generally be seen radiologically as sinuous, double-contoured lines running with the cortical convolutions on the affected side, but this change is generally absent in infancy and, in a proportion or cases, throughout life. However, intracranial calcification is generally visible by CT scanning, especially when enhanced by contrast injection, within the first few months of life[68]. Gadolinium-enhanced MRI scans are now considered to be the superior technique for the detection of the angiomatosis, definition of its extent and of associated vascular anomalies, assessment of the degree of parenchymal atrophy and of ischaemic damage[69].

Although the primary management for seizures is with pharmacologic agents, surgical therapy may become necessary. Hemispherectomy is often advised for patients with intractable seizures and unihemispheric involvement[70].

KLIPPEL - TRENAUNAY SYNDROME:

It is a sporadic disorder characterized by the triad of vascular malformations, venous varicosity, and hyperplasia of soft tissue and bone. The vascular malformation is most often a capillary malformation of the portwine stain type. The lower extremity is the most common location

involved[71]. When arteriovenous malformations are also present; patients have to be invariably referred to as having Parkes-Weber syndrome[34].

However, in addition, it is characteristic for other, often large or complex vascular malformations to co-exist with the port-wine stain. Perhaps lymphangioma circumscriptum is the most typical of all, but deep lymphatic and/or venous malformations are also relatively common[72]. The latter are most likely to have been present since birth. Lymphoedema is also common, and may be accompanied by recurrent bouts of cellulitis.

Complications include thrombophlebitis, coagulopathy, compensatory scoliosis and hip dislocation[34]. Treatment is mainly supportive. The clearest indication for surgical therapy is leg length discrepancy, which is projected to exceed 2 cms at skeletal maturity and which can be treated with epiphysiodesis in growing child[73].

PROTEUS SYNDROME:

The Proteus syndrome comprises an association of asymmetrical overgrowth of almost any part of the body, verrucous epidermal naevi, infantile haemangiomas and lipoma-like subcutaneous hamartomas[74]. Macrodactyly has been regarded as particularly characteristic, but should not be considered necessary to the diagnosis. The rugose or cerebriform overgrowth of the plantar and/or palmar soft tissues on a hypertrophied foot and/or hand seems to be highly distinctive. Macrocephaly and/or an

excessive linear growth rate are also common findings. Other skin findings have included café-au-lait macules and macular hypopigmentation, which may be of a linear or whorled type[74].

Other non-cutaneous findings have included skeletal abnormalities, such as exostoses, kyphosis, scoliosis and spinal canal stenosis leading to spinal cord compression, ocular abnormalities including congenital blindness, epibulbar tumours, enlargement of the eye, cataract and strabismus, misshapen teeth, hypodontia etc[6].

PHAKOMATOSIS PIGMENTOVASCULARIS:[75]

The word phakomatosis has come to imply simultaneous involvement by a developmental malformation syndrome of eye, skin and CNS. The rather clumsy term, phakomatosis pigmentovascularis, has been proposed for a syndrome combining vascular malformations of port-wine stain type, oculocutaneous melanosis and CNS manifestations such as seizures and hemiplegia .

Type I: port-wine stain and linear epidermal naevus

Type II: port-wine stain and dermal melnocytosis

Type III: port-wine stain and naevus spilus

Type IV: port-wine stain, dermal melanocytosis and naevus spilus

Cobb syndrome:

In Cobb syndrome (cutaneomeningospinal angiomatosis), a cutaneous vascular lesion in the skin overlying the spine, is associated with vascular malformations (venous or arteriovenous) in the subjacent spinal meninges[34].

Wyburn-Mason syndrome:

Wyburn-Mason syndrome (unilateral retinocephalic syndrome), also known as Bonnet-Dechaume-Blanc syndrome, manifests as facial capillary malformations associated with unilateral AVM of the retina and the intracranial optic pathway. Capillary malformations may occur anywhere on the ipsilateral face (not just the eyelids or periorbitally), and they may have associated facial hypertrophy or occasional involvement of the optic chiasm, the hypothalamus, the midbrain, and the basal ganglia, with associated mental retardation or neurologic signs and symptoms[6].

AIM OF THE STUDY

1. To study the incidence of hemangiomas and vascular malformations.

2. To study the age of onset of hemangiomas and vascular malformations.

3. To study the sex distribution of hemangiomas and vascular malformations.

4. To study the familial incidence of hemangiomas.

5. To study the distribution of lesions.

6. To study the complications.

7. To study the associations.

MATERIALS AND METHODS

Patients attending the Department of Dermatology, Madras Medical College during the period August 2007- September 2009 were screened for hemangiomas and vascular malformations and those were the subjects of a descriptive study. The clinical findings were recorded in a proforma. The parameters noted were age, sex, age of onset, reason for visiting the hospital, family history, duration of lesion, site of involvement, morphology of lesions, number of lesions, and associated findings. In addition to the presenting symptoms, a skin biopsy was done wherever necessary. Relevant investigations were carried out for any systemic association. The results obtained were tabulated and analyzed.

OBSERVATIONS AND RESULTS

A total of 52,369 cases attended the dermatology OPD during the study period from August 2007 to September 2009. Out of these, 56 cases (0.11%) were found to have vascular naevi. Thirty six of them were hemangiomas and twenty cases were port-wine stains.

Presenting age group of vascular naevi:

Of the 56 cases with vascular naevi, patients with hemangioma presented early and were mostly within 5 years of age. Vascular malformations though present since birth, the presenting age group was mostly above 10 years.

Table 1

Vascular naevi	0-5 years	5-10 years	>10 years
Hemangioma	34	2	-
Vascular Malf.	1	1	18

HEMANGIOMA:

Incidence:

Hemangiomas accounted for 36 (64.29%) of all the 56 cases of vascular anomalies.

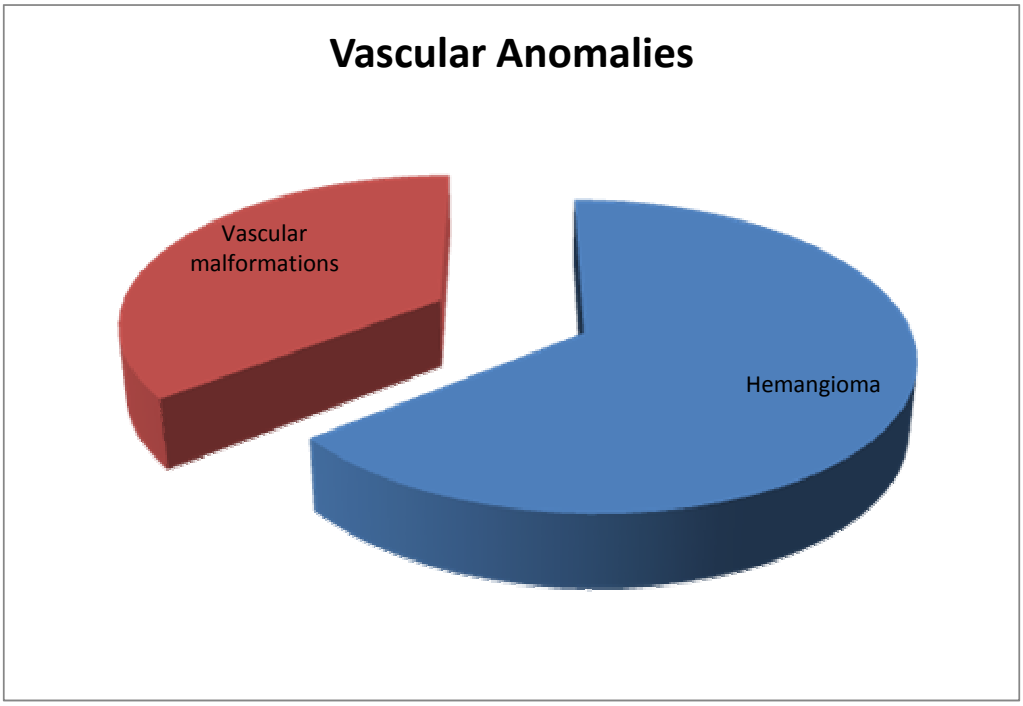


Figure 1

AGE DISTRIBUTION:

Of the 36 cases in the study, 30 cases had lesions at birth, 4 cases had appearance of the lesion at 1st month, one case had appearance of lesion at 2nd month, and one case had development of lesion by 3rd month.

Table 2

Age of onset	Male	Female	Percentage
At birth	6	24	83.33%
1st month	1	3	11.11%
2nd month	1	0	2.78%
3rd month	0	1	2.78%

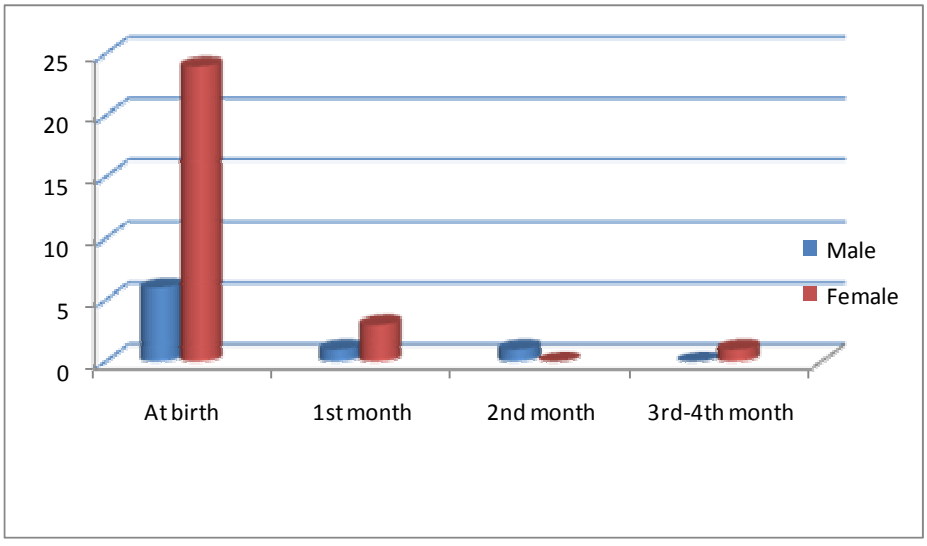


Figure 2

SEX DISTRIBUTION:

There was a female preponderance with female patients numbering 28(77.78%) and male patients numbering 8(22.22%) of the total 36 cases.

Table - 3

Sex	No. of cases	Percentage
Male	8	22.22%
Female	28	77.78%

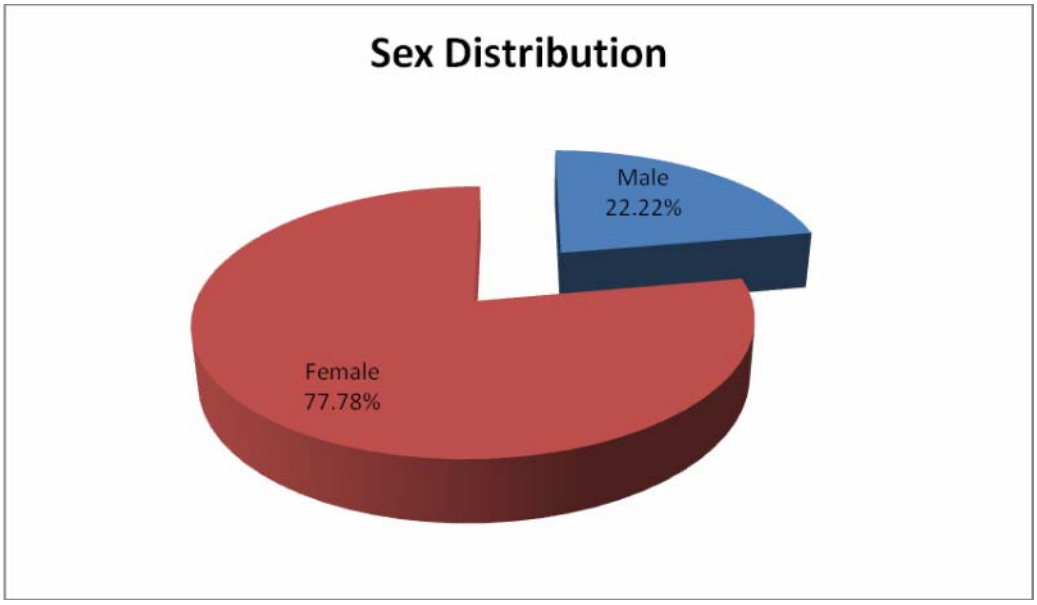


Figure 3

FAMILY HISTORY:

Out of the 36 cases a positive family history in either the parents or the siblings was present in 4 cases (11.11%).

BIRTH (NATAL) HISTORY:

Among the observed 36 cases, 7(19.44%) had a history of pre term birth occurring before 36 weeks. One case out of these 7 cases was delivered even before 32 weeks. The birth weight obtained by history accounted that 4 cases (11.11%) were between 1500gm- 2500gm and 1 case (2.77%) was even below 1500gm and the infant was intervened with oxygen therapy due to faulty breathing.

Table 4

Time of delivery	No. of cases	Percentage
< 32 weeks	1	2.78%
32-36 weeks	6	16.67%
>36 weeks	29	80.55%

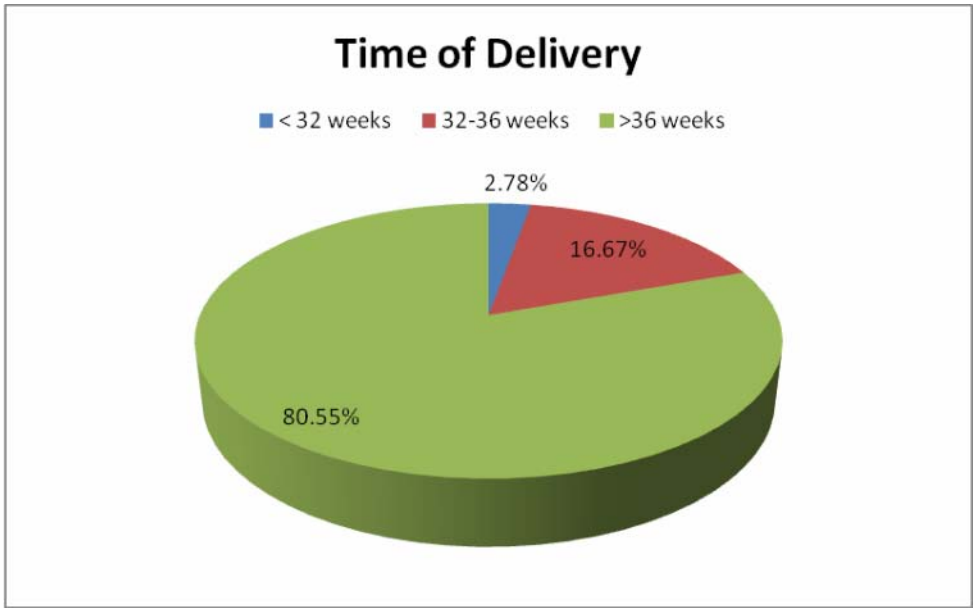


Figure 4

Table 5

Birth weight	No. of cases	Percentage
< 1500gm	1	2..78%
1500-2500gm	4	11.11%
2500gm>	31	86.11%

Figure 5

NO. OF LESIONS:

Single lesion was present in 32 cases (88.89%) while rest of the 4 cases (11.11%) had multiple lesions.

Table 6

No.of lesions	No. of cases	Percentage
Single	32	88.89%
Multiple	4	11.11%

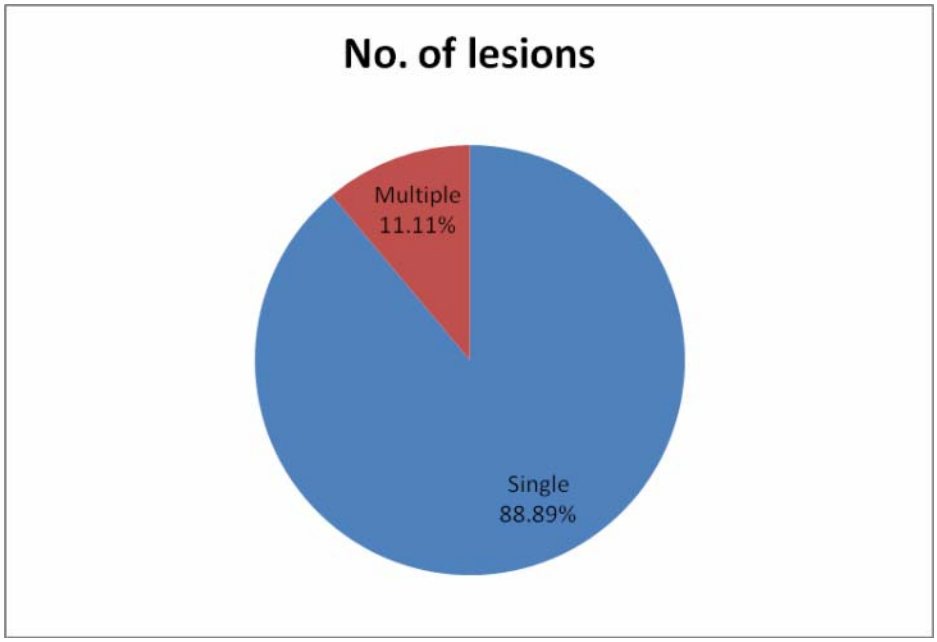


Figure 6

LESION SUBTYPE:

Localized lesions were the most commonly encountered type in 24 cases (66.67%). Segmental type was seen in 5 cases (13.89%), indeterminate type was observed in 6 cases (16.67%) and 1 case (2.78%) had multifocal type. Complications were mostly seen in segmental type.

Table 7

Lesion type	No. of cases	Percentage
Localised	24	66.67%
Segmental	5	13.89%
Indeterminate	6	16.67%
Multifocal	1	2.78%

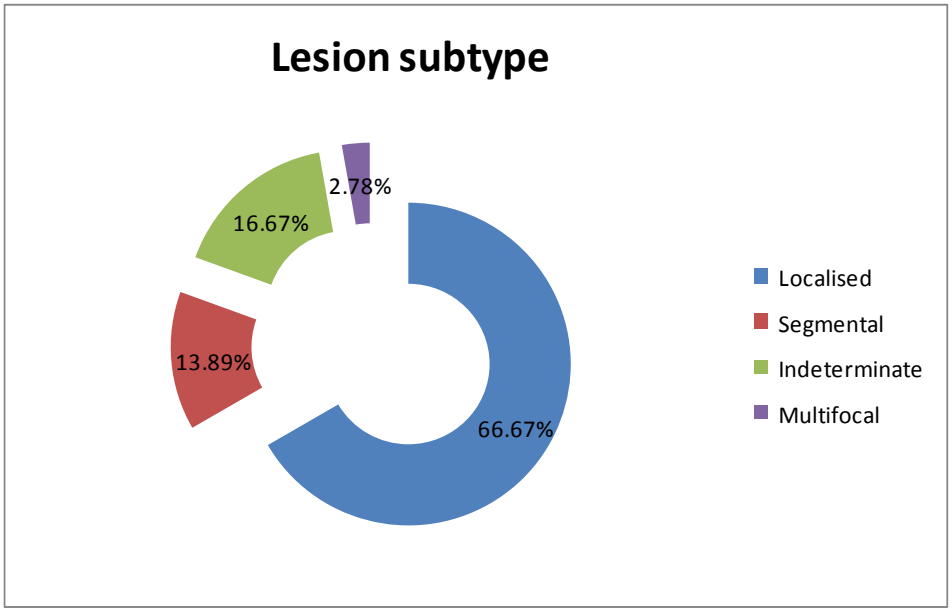


Figure 7

DISTRIBUTION OF LESIONS:

The most common site of involvement is head and neck in 16 cases followed by trunk in 9 cases and extremities in 9 cases. One case had the involvement of genitalia. One case had mutifocal involvement.

Table 8

Area of involvement	No. of cases	Percentage
Head and neck	16	44.44%
Trunk	9	25%
Extremities	9	25%
Genitalia	1	2.78%
Multiple	1	2.78%

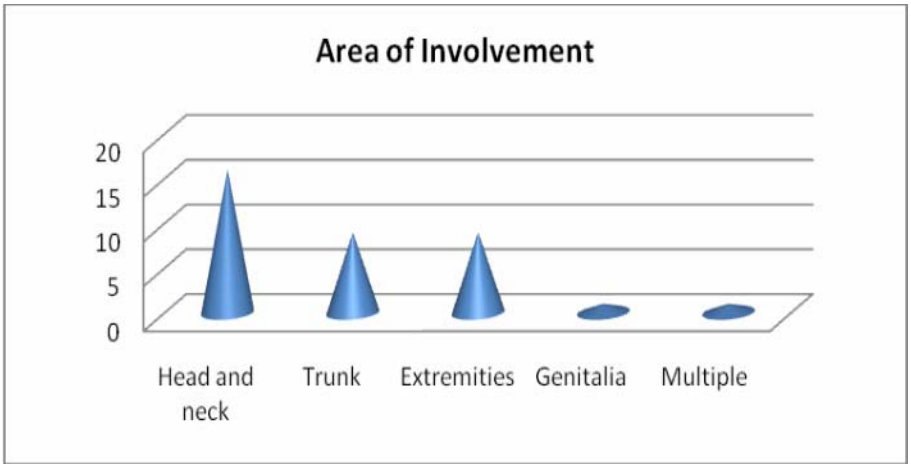


Figure 8

COURSE OF THE LESION:

In our study out of the 36 cases, 11 cases (30.56%) were in progressive phase, 21 cases (58.33%) were in non-involuting phase and only 4 cases (11.11%) were in the involuting stage while no case had complete involution during the study period. 2 cases were operated owing to their bleeding and ulcerative complications.

Table 9

Course	No. of cases	Percentage
Progressive	11	30.56%
Non-involuting	21	58.33%
Regressive	4	11.11%

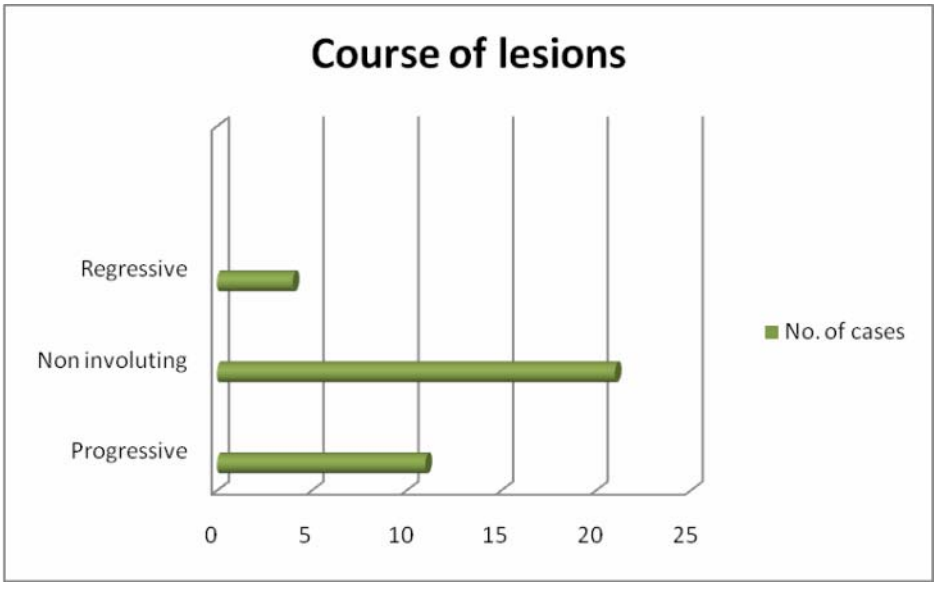


Figure 9

COMPLICATIONS:

In our study out of 36 cases, 11 cases presented with various complication. 6 cases (16.67%) had ulceration, 3(8.33%) had bleeding complication, feeding and breathing difficulty in 2(5.56%) and 1 case had occlusion of eye.

Table 10

Complications	No. of cases(n=36)	Percentage
Ulceration	6	16.67%
Bleeding	3	8.33%
Feeding and Breathing difficulty	2	5.56%
Vision impairment	1	2.78%

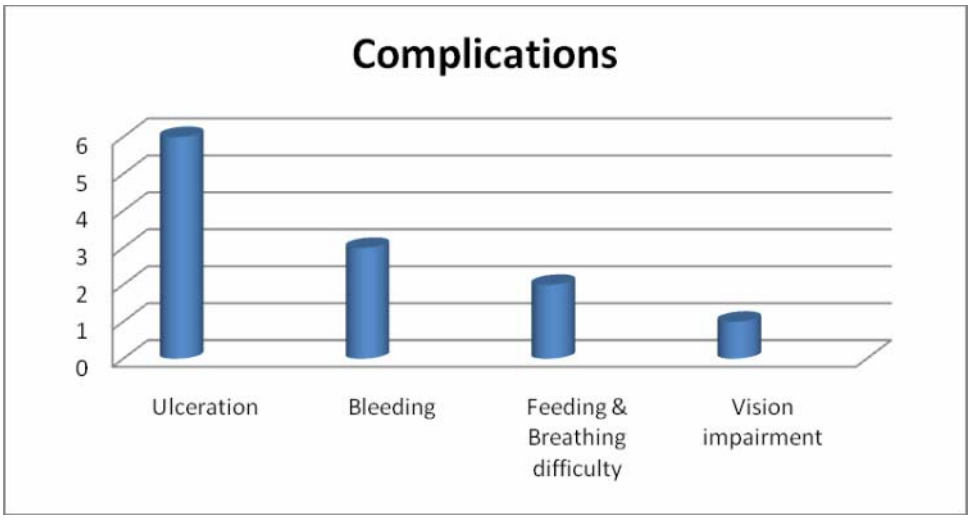


Figure 10

RARER ASSOCIATIONS AND PRESENTATIONS:

One case was associated with occlusion of vision and with hydrocephalus and CT showed posterior fossa malformation in the form of Dandy Walker malformation. Cardiac evaluation of the child was normal.

One case presented with hemangioma involving the left cheek with stridor. MRI revealed subglottic extension of hemangioma and the patient was referred to ENT department and was suggested observation without any active intervention till 3 years of life. During the one year follow up, child was relieved of stridor and was comfortable.

INVESTIGATIONS:

Baseline investigations were done in all the patients and they were within normal limits.

X-ray and CT scan were taken in specific cases and one case showed Dandy Walker malformation.

MRI was done in 2 cases and one case revealed subglottic involvement.

Biopsy was done in 3 patients and it was consistent with the diagnosis of hemangioma.

VASCULAR MALFORMATIONS

Incidence:

Vascular malformations accounted for 20 cases (35.71%) of all the 56 vascular anomalies observed.

Age of onset:

All the 20 cases in our study had the presence of lesions since birth.

Sex distribution:

Of the 20 cases in the study 9 were males (45%) and 11 were females (55%).

Table 11

Sex	No. of cases	Percentage
Male	9	45%
Female	11	55%

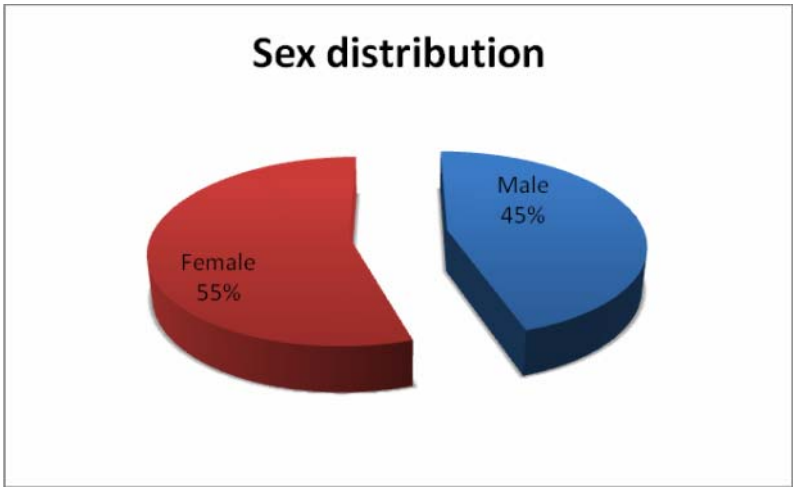


Figure 11

DISTRIBUTION OF LESIONS:

Out of the 20 cases, 15 cases (75%) had the involvement of face, followed by extremity involvement in 4 cases (20%), while 1case (5%) had involvement of the back.

Table 12

Site of involvement	No. of cases	Percentage
Face	15	75%
Extremities	4	20%
Back	1	5%

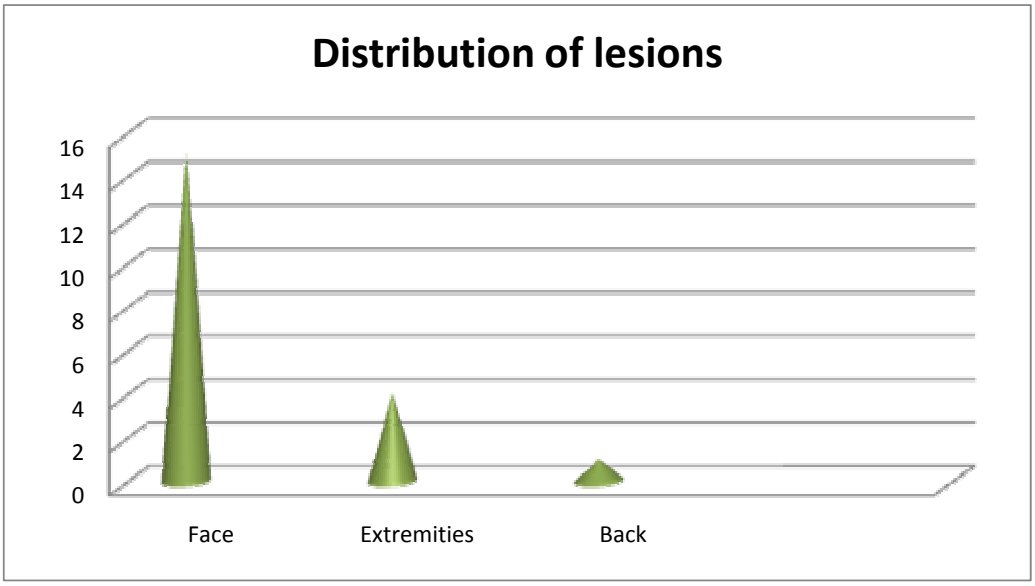


Figure 12

NO. OF DERMATOME INVOLVEMENT:

In our study 7 cases (35%) had unidermatomal involvement and 13 cases (65%) had more than one dermatomal involvement.

Table 13

	No. of cases	**Percentage**
Unidermatome	7	35%
Multidermatome	13	65%

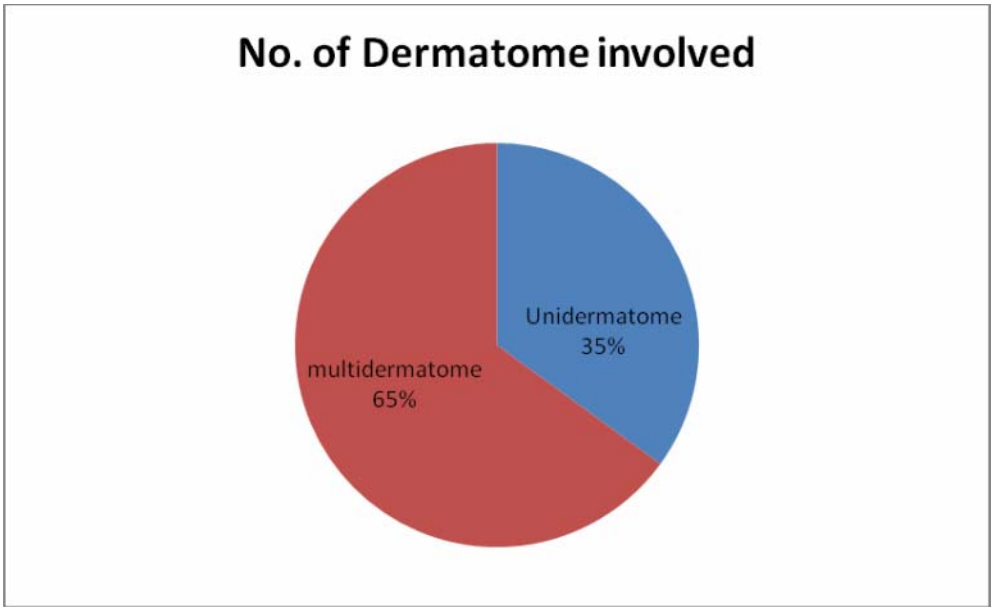


Figure 13

DISTRIBUTION OF FACIAL LESION:

Of the facial involvement in 15 cases, extensive and bilateral involvement was present in 3 cases (20%), the rest 12 cases (80%) had unilateral involvement.

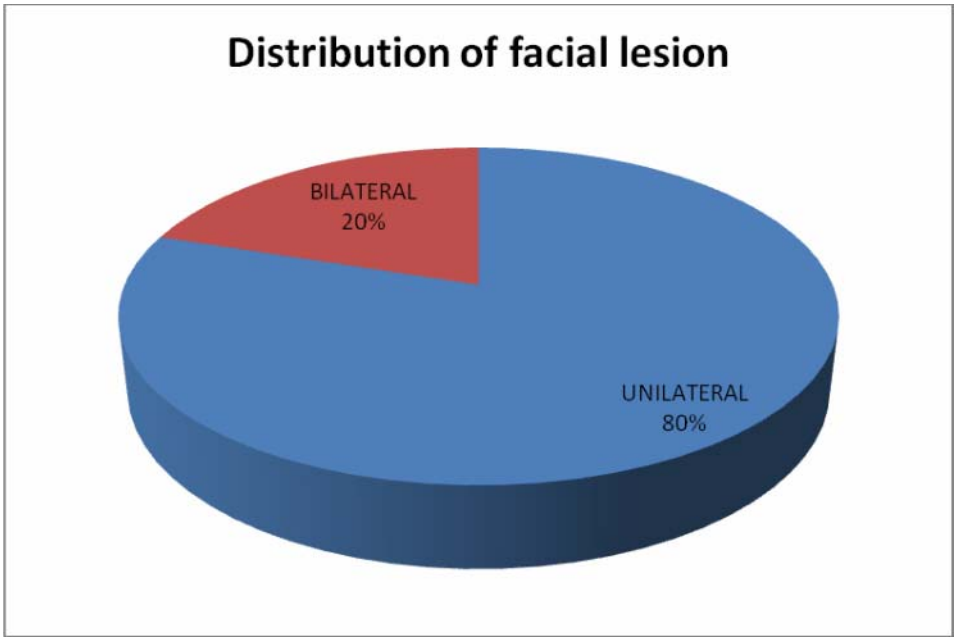


Figure 14

MUCOSAL INVOLVEMENT:

Of the 15 cases with facial involvement adjacent mucosa was involved in 6 cases (40%).

TRIGEMINAL NERVE INVOLVEMENT:

Portwine stain was mostly observed in the maxillary distribution alone in 8 cases (53.33%) and ophthalmic branch was involved in 2 cases (13.33%), maxillary and ophthalmic branch was involved in 1 case (6.67%) and all the three branches were involved in 4 cases (26.67%).

Table 14

Trigeminal Branch	No. of cases	Percentage
Ophthalmic	2	13.33%
Maxillary	8	53.33%
Oph, Max	1	6.67%
Oph, Max, Man	4	26.67%

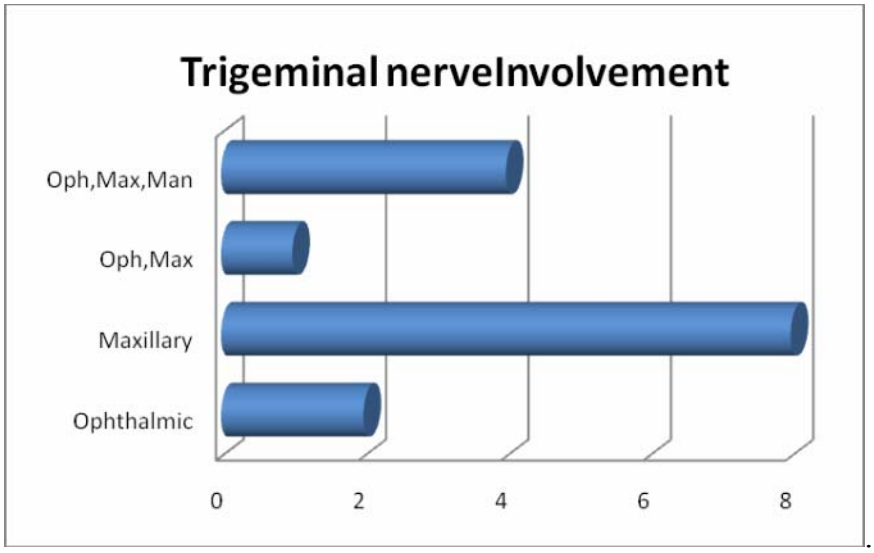


Figure 15

COMPLICATIONS ASSOCIATED WITH FACIAL INVOLVEMENT:

Of the 15 cases with facial involvement, 5 cases (33.33%) had either ocular complication or CNS involvement or both. Out of the 3 cases with bilateral distribution, 2 cases (66.67%) and of the 12 cases with unilateral distribution, 1 case (8.33%) had glaucoma. Among the 3 cases with extensive & bilateral involvement, 2cases (66.67%) and 1case (8.33%) of unilateral distribution had a positive history for CNS involvement in the form of seizures. But all the three cases had normal CT finding.

Table 15

Distribution of lesions / Complications	No. of cases
Unilateral with CNS inv.	1
Unilateral with Glaucoma	1
Bilateral with CNS inv.	1
Bilateral with glaucoma	1
Bilateral with CNS inv and glaucoma	1

OTHER PRESENTATIONS:

Klippel Trenaunay Syndrome was noted in two of the patients. These patients had increased limb length and increased girth compared to the normal limb and both cases had gait disturbance. Venous varicosity was evident in the affected limb in both cases by Doppler study.

Phakomatosis pigmentovascularis was observed in three cases. One case was associated with naevus of ota and congenital melanocytic naevi. One case was associated with congenital melanocytic naevi and the other case was associated with linear epidermal naevus.

INVESTIGATIONS:

Baseline investigations were done in all the patients and they were within normal limits.

X- Ray of the affected part was taken in selective cases and in 2 cases with Klippel Trenaunay syndrome there was increased limb length with soft tissue swelling.

MRI was done in 2 patients and in one patient it revealed a pituitary microadenoma. CT scan was done in selective patients and was within normal limits. Ophthalmic opinion was sought in patients with facial involvement and among them three patients were found to have glaucoma.

DISCUSSION

In our study 56 cases presented with vascular naevi. The most common presenting age group of hemangiomas was below 5 years. Vascular malformations though present since birth, presenting age was only after 10 years of age.

HEMANGIOMAS

Infantile hemangiomas are the commonest tumors of infancy, with a prevalence of approximately 1-3% after the first few days of life and approximately 10% by the end of the first year. In our study, hemangiomas were seen in 36 cases.

Hemangiomas are often absent or small at birth and grow rapidly at a rate beyond the child's growth followed by slow involution, often leading to complete regression. In the study of 327 patients of hemangioma by *Chiller et al.*[76] a total of 36% of patients had lesions at birth, whereas 40% developed lesions within the first month of life. In *Senthilkumar et al.*[77] study of 17 cases, 13 (76.5%) cases were present at birth and remaining 4 (21.1%) cases appeared up to 1 year of age. In our study of 36 cases of hemangioma, 30(83.33%) cases were present at birth and of remaining 6 (16.67%) cases, 4 cases had appearance of lesion at 1 month, 1 case started developing lesion at 2nd month and 1 case had lesion from 3rd month. Thus in our study, almost all cases developed

their lesions within three months of life, which is comparable to other studies in which cases also there was an early onset of hemangioma.

Girls are more frequently affected than boys in the ratio of 3:1[24], except in small preterm infants where it is closer to 1:1. In *Chiller et al.* study, there were 79% girls and 21% boys with a female to male ratio of 3.7:1. In *Senthilkumar et al.* study females (76.5%) were much more frequently affected than males (23.5%), with a sex ratio of 3.3:1. Similarly, we found females 28(77.78%) to be more frequently affected than males 8(22.22%) with a sex ratio of 3.5:1. *Chiller et al.* documented a positive family history of hemangioma in 10% cases, whereas in our study there were 4(11.11%) patients with family history of hemangioma.

The prevalence of infantile hemangiomas at 1 year in preterm infants was shown to be inversely related to gestational age at birth, and it occurs more commonly in infants born before 36 weeks[25]. In our study 7 cases (19.44%) were born before 36 weeks and among the 7 cases, one case was born even before 32 weeks. Hemangioma also was also found to be increasing in inverse relationship to birth weight with increased prevalence in infants weighing less than 1500 gm at birth[25]. In our study 4(11.11%) cases were found to have low birth weight between 1500-2500gm. Only 1 case (2.77%) had birth weight less than 1500gm.

Mostly hemangiomas occur as a single lesion[78]. In *Senthilkumar et al.* study only 8 (47.1%) were solitary, the remaining 9 (52.9%) were

multiple. But in our study 32(88.89%) were solitary and the remaining 4(11.11%) were multiple and this is in concurrence with other studies. Of the 4 cases, 3 cases had more than 2 lesions and 1 case had more than 10 lesions.

In the study of Hemangiomas of infancy, *Chiller et al*. made a diagram (Figure 15) of the human body and gave a numerical value to each anatomic location. With the help of photographs of individual lesions or written descriptions, they mapped the individual lesions. Finally, they classified the lesions into localized, segmental, indeterminate, and multifocal. Localized lesions demonstrated clear spatial containment, usually with involvement of only 1 or 2 mapped sites. Segmental lesions demonstrated linear and/or geographical localization over a specific cutaneous territory and were usually associated with at least some plaque-like features. They were often unilateral and usually sharply demarcated at the midline, but there were exceptions, particularly nasal and lip lesions. The indeterminate lesions were hemangiomas that could not be confidently categorized as either localized or segmental. Hemangiomas were considered multifocal if the infant had eight or more individual noncontiguous lesions of any morphologic characteristic. In the study of 327 cases of hemangioma by *Chiller et al*., 227 cases were of the localized type, 78 cases were of the segmental type, 34 cases were of the indeterminate type, and 12 cases were of the multifocal type. In *Senthilkumar et al* study of 17 cases, 15

cases were of localized type and 2 cases were of multifocal type. In our study also localized type was most commonly observed among 24 cases (66.67%). Segmental type was seen in 5 cases (13.89%), indeterminate type was observed in 6 cases (16.67%) and 1 case (2.78%) had multifocal type. Of these, cases with segmental distribution had an increased incidence of complications which is in coherence with other studies.

Although hemangiomas may occur on any part of the body, they demonstrate a striking predisposition for the head and neck regions. In a large series, 60% of hemangioma occurred on the head and neck, followed by 25% on the trunk, and 15% on extremities[79]. In our study hemangiomas were distributed in head and neck in 16(44.44%), trunk 9(25%), extremities 9(25%), genitalia in 1(2.78%), and multiple sites were involved in 1 case (2.78%). Thus as far as, single site of involvement is concerned, the most commonly involved site was head and neck, followed by trunk and extremities, which is comparable to earlier studies.

The growth characteristics of hemangioma are often divided into 3 phases- proliferating, involuting, and involuted. In *Senthilkumar et al.* study of 17 cases of hemangioma, 15 (88.2%) were progressive and two (11.8%) were non-involuting. Out of these 17 progressive cases, 11 (64.7%) were progressing gradually and remaining 4 (21.1%) were progressing rapidly. In our study of 36 cases, 4 cases (11.11%) were in the involuting phase while 11 cases (30.56%) were in progressive phase

and 21cases (58.33%) were in non involuting phase. Of the 4cases in involuting phase, involution started after 1 year of age in 3 cases and after the 2nd year in 1 case.

Complications of hemangioma may result from their location, size, or rapid, proliferating phase. In the study of 327 cases by *Chiller et al.* 40% of the lesions had some type of complication. Ulceration was observed in 75 lesions along with bleeding (usually minor) in 27, cutaneous infection in 14, and significant pain in 12. In *Senthilkumar et al.* study, four (23.5%) cases had some type of complication. Those complications included ulceration in all four cases and associated infection in a solitary case. In our study complications were present in 11(30.56%), out of which 6(16.67%) had ulceration, 3(8.33%) had bleeding complication, feeding & breathing difficulty in 2(5.56%) and 1(2.78%) had occlusion of vision. Thus, ulceration was the most common complication in our study as in other studies and it occurred following trauma. In our study complications were common with children born either preterm or with low birth weight or both.

In *Chiller et al.* study, the mucous membrane was involved in 10% cases[76]. In our study adjacent mucosal involvement was present in 4 cases (11.11%). But isolated mucosal involvement was not seen.

Associations observed in our study were, one case with hydrocephalus with occlusion of eye and other case showed subglottic

involvement in MRI. Excision was done in 2 patients with repeated ulceration. Patient did not develop recurrence during the 1 year follow up. Child with subglottic involvement was referred to ENT department and was suggested observation and no active intervention till 3 years of age. During the follow up period child was relieved of stridor.

VASCULAR MALFORMATIONS

Vascular malformations are localized or diffuse errors of embryonic development of which port-wine stain is a common vascular anomaly that is present at birth and persists throughout life. Out of the 56 cases of vascular naevi in our study, portwine stain was observed in 20 cases (35.71%). In our study all the 20 cases had the lesion since birth which is compatible with the literature. In *B .Tallman et al*[80] study of portwine stain in 310 patients, 68% had more than one dermatome involved. In our study 7 cases (35%) had unidermatomal involvement and 13 cases (65%) had more than multidermatomal involvement.

In *B .Tallman et al* study of 310 patients, extensive involvement with port-wine stain over the trunk and extremities as well as the head and neck, was observed in 12% and of the facial lesions 85% had unilateral and 15% had a bilateral distribution of their port-wine stain. In *Juliette M. H.et al*[81] study of the prognosis of bilateral facial capillary malformation compared with that of unilateral facial port-wine stain in 350 patients 7.71% of cases had bilateral distribution. In the series of 121 cases

reported by *Bioxeda*[82] and colleagues, patients with bilateral distribution represented 14% total population of those with CM. In our study face was the most common site involved in 15 cases (75%), followed by extremity involvement in 4 cases (20%) while 1 (5%) had involvement of the back. Of the facial involvement in 15 cases, extensive and bilateral involvement was present in 3 cases (20%), the rest 12 cases (80%) had unilateral involvement. The adjacent mucosal involvement was present in 6 cases (40%) out of the 15 cases with facial involvement.

In *Bioxeda et al* study of 121 cases, 88% had involvement of maxillary division of trigeminal nerve either isolated or along with ophthalmic and mandibular division (Figure 16). In our study also Portwine stain had isolated involvement of maxillary distribution in 8 cases (53.33%) and ophthalmic branch was involved in 2 cases (13.33%), maxillary and ophthalmic branch was involved in 1 case (6.67%) and all the three branches were involved in 4 cases (26.67%). The patients with CNS or Ocular complications or both had preferential distribution of the portwine stain over the maxillary branch of the trigeminal nerve.

In *B .Tallman et al* study 8% of all patients with trigeminal port-wine stain had evidence of eye and/or central nervous system (CNS) involvement. In our study of the 15 cases with facial involvement 5 cases (33.33%) had ocular involvement or CNS involvement or both.

In *B .Tallman et al* study 24% of those with bilateral trigeminal nerve port-wine stains had eye and/or CNS involvement compared with 6% of those with unilateral lesions. In the *Bioxeda et al* study 26% of the patients with bilateral lesion had epilepsy, compared with 14% of those with unilateral lesions. In our study out of the 3 cases with bilateral distribution, 2 cases (66.67%) and of the 12 cases with unilateral distribution, 1 case (8.33%) had glaucoma. Among the 3 cases with extensive & bilateral involvement, 2 cases (33.33%) and 1case (8.33%) of unilateral distribution had a positive history for CNS involvement in the form of seizures. But all the three cases had normal CT finding.

In our study 2 cases of Klippel Trenaunay Syndrome was observed and both cases had limb length discrepancy and also an increased limb girth. Phakomatosis pigmentovascularis was observed in 3 cases in our study, of which one case was found to be associated with linear epidermal naevi while one case was associated with both congenital melanocytic naevi and nevus of ota and other case had an association with congenital melanocytic naevi alone.

CONCLUSION

- Hemangiomas and vascular malformations were a rare occurrence constituting only 0.11% of all new cases attending the Dermatology outpatient department during the study period.

- The incidence of hemangiomas was almost twice as much as that of vascular malformations.

- Most of the hemangiomas had onset at birth while all vascular malformations were present since birth.

- Hemangiomas had a female predominance, while in vascular malformations there was almost an equal sex distribution.

- Familial incidence of hemangiomas was encountered in 11.11% cases.

- The most common site of occurrence in hemangioma was head and neck followed by trunk, extremities, and genitalia; while in vascular malformation face was the most commonly involved site followed by extremities and trunk.

- Hemangiomas commonly presented with single lesion, and most cases were either in progressive or non involuting phase. Multidermatomal involvement was observed more often in vascular malformations.

- Localized type of hemangiomas was most commonly observed while segmental type was most commonly associated with complications.

- Port wine stain occurred most commonly over the distribution of maxillary division of trigeminal nerve. Patients with CNS or ocular complications or both had preferential involvement of maxillary branch.

- Most frequently encountered complication in hemangiomas was ulceration followed by bleeding, feeding difficulty and vision impairment. In vascular malformations, seizures and glaucoma were the complications noted.

- Complications of hemangiomas were found to be common among children born either preterm or low birth weight or both.

- Hydrocephalus and subglottic involvement was noted in 2 cases of hemangioma; while 3 cases of Phakomatosis pigmentovascularis and 2 cases of Klippel Trenaunay were observed in patients with vascular malformation.

REFERENCES

1. Mulliken JB, Glowascki J: Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. Plastic reconstructive surg , 1982; 69:412.

2. Godanich IF, Campanacci M. Vascular hamartomata and infantile angioectatic osteohyperplasia of the extremities. J Bone Joint Surg. 1962; 44A:815.

3. Metry D. Update on hemangiomas of infancy. Curr Opin Pediatr. 2004; 16:373-37.

4. Enjolras o, Mulliken JB: Vascular tumors and vascular malformations. Adv Dermatol , 1998; 13:375.

5. Mulliken JB, Young AE: Vascular Birthmarks: Hemangiomas and Malformations. Philadelphia, Saunders 1988: 41-62.

6. D.J.Atherton,C.Moss: Rook's Textbook of Dermatology, 7th edition:15.39-15.87.

7. Cheung DS, Warman ML, Mulliken JB. Hemangioma in twins. Ann Plast Surg. 1997; 38:269–274.

8. Blei F, Walter J, Orlow SJ. Familial segregation of hemangiomas and vascular malformations as an autosomal dominant trait: a rare genetic disorder. Arch Dermatol. 1998; 134:718–722.

9. Walter JW, et al. Genetic mapping of a novel familial form of infantile hemangioma. Am J Med Genet. 1999; 82:77–83.

10. Boye E, et al. Clonality and altered behavior of endothelial cells from hemangiomas. J Clin Invest. 2001; 107:745–752.

11. Yu Y, Fuhr J, Boye E, et al. Mesenchymal stem cells and adipogenesis in hemangioma involution. Stem Cells. Jun 2006; 24(6):1605-12.

12. Amir J, Metzker A, Krikler R et al. strawberry hemangioma in preterm infants. Pediatr Dermatol 1987; 3:331-2.

13. Sasaki GH, Pang CY, Wittliff JL. Pathogenesis and treatment of infant skin strawberry hemangiomas: clinical and in vitro studies of hormonal effects. Plas Reconstr Surg 1984; 73:359-68.

14. North PE, Waner M. GLUT1, a newly discovered immunohistochemical marker for juvenile hemangiomas. Hum Pathol. 2000; 31:11–22.

15. North, P.E., et al. 2001. A unique microvascular phenotype shared by juvenile hemangiomas and human placenta. Arch. Dermatol. 2001; 137:559-570.

16. Kaplan P, et al. Malformations and minor anomalies in children whose mothers had prenatal diagnosis: comparison between CVS and amniocentesis. Am J Med Genet. 1990; 37:366–370.

17. Burton BK, Schulz CJ,et al. An increased incidence of haemangiomas in infants born following chorionic villus sampling (CVS). Prenat Diagn. 1995; 15:209–214.

18. Banks RE, Forbes MA, Searles J, et al. Evidence for the existence of a novel pregnancy-associated soluble variant of the vascular endothelial growth factor receptor, Flt-1. Mol Hum Reprod. Apr 1998; 4(4):377-86.

19. Hornig C, Barleon B,et al. Release and complex formation of soluble VEGFR-1 from endothelial cells and biological fluids. Lab Invest. Apr 2000; 80(4):443-54.

20. Jinnin M, Medici D, Park L, et al. Suppressed NFAT-dependent VEGFR1 expression and constitutive VEGFR2 signaling in infantile hemangioma. *Nat Med*. Nov 2008; 14(11):1236-46.

21. Klagsbrun M, Sasse J, Sullivan R et al. Human tumor cells synthesize an endothelial cell growth factor that is structurally related to basic fibroblast growth factor. Proc Natl Acad Sci USA 1986; 83:2448-52.

22. Glowascki J, Mulliken JB. Mast cells in hemangiomas and vascular malformations. Pediatrics 1982; 70:48-51.

23. John P.Connors, John B. Mulliken. Rutherford Textbook of Vascular surgery: 1626-43.

24. Mulliken JB, Fishman SJ, Burrows PE: Vascular anomalies. Curr Probl Surg 2000; 37:520.

25. Powell TG, West CR, Pharaoh POD et al. Epidemiology of strawberry hemangioma in low birth weight infants. Br J Dermatol 1987; 116:635-41.

26. Margileth AM, Museles M: Cutaneous hemangiomas in children: Diagnosis and conservative management. JAMA 1965; 194:523.

27. Bowers RE, Graham EA, Tomlinson KM: The natural history of the strawberry nevus. Arch Dermatol 1960; 82: 667-80.

28. Kim HJ, Colombo M, Frieden IJ. Ulcerated hemangiomas: clinical characteristics and response to therapy. J Am Acad Dermatol 2001, 44:962-72.

29. Kauffman SL, Stout AP. Malignant hemangioendothelioma in infants and children. Cancer 1961; 14:1186-96.

30. Kauffman SL et al. Hemangiopericytoma in children. Cancer 1960; 13:695-710.

31. Howell DM, Gumbiner CH, Martin GEO. Congestive cardiac failure due to giant cutaneous hemangioma. Clin Pediatr(phila) 1984; 23:504-6.

32. Zuckerberg LR, Nikloff BJ, Weiss SW: Kaposiform hemangioendothelioma ofinfancy and childhood: An aggressive neoplasm associated with Kasabach-Meritt syndrome and lymphangiomatosis. Am J Surg Pathol 1993; 17:321.

33. Enjolras O, Wassef M, Mazoyer E, *et al*. Infants with Kasabach-Merritt syndrome do not have "true" hemangiomas. J Pediatr 1997; 130:631-640.

34. Hurwitz clinical pediatric dermatology, 3rd edition: 307-330.

35. Thomson HG, Ward CM et al Hemangiomas of eyelid:visual complications and prophylactic concepts. Plastic Reconstr Surg 1979; 63:641-7.

36. Orlow SJ, Isakoff MS, Blei F. Increased risk of symptomatic hemangiomas of the airway in association with cutaneous hemangiomas in a' beard' distribution. J Pediatr 1997; 131:643-6.

37. Frieden IJ, Reese V, Cohen D. PHACE syndrome: the association of posterior fossa brain malformations, hemangiomas, arterial anomalies, coarctation of aorta and cardiac defects, and eye abnormalities. Arch Dermatol 1996; 132:307-11.

38. Dubois J, Patriquin HB, Garel L, et al.Soft tissue hemangiomas in infants and children: Diagnosis using Doppler sonography. AJR Am J Roentgenol 1998; 171:247.

39. Meyer JS, Hoffer FA et al. Biological classification of soft tissue vascular anomalies: MR correlation. AJR Am J Roentgenol 1991; 157:559.

40. Morelli JG, Tan QT,et al. Treatment of ulcerated hemangiomas in infancy. Arch Pediatr Adolesc Med 1994; 148:1104.

41. Sadan N, Wolach B. Treatment of hemangiomas of infants with high doses of prednisone. J Pediatr. Jan 1996; 128(1):141-6.

42. Garden JM, Bakus AD, Paller AS. Treatment of cutaneous hemangiomas by the flashlamp-pumped pulsed dye laser: prospective analysis. J Pediatr. Apr 1992; 120(4 Pt 1):555-60.

43. Poetke M, Philipp C, Berlien HP. Flashlamp-pumped pulsed dye laser for hemangiomas in infancy: treatment of superficial vs mixed hemangiomas. Arch Dermatol. May 2000; 136(5):628-32.

44. Sie KC, McGill T, Healy GB. Subglottic hemangioma: ten years' experience with the carbon dioxide laser. Ann Otol Rhinol Laryngol. Mar 1994; 103(3):167-72.

45. Achauer BM, Chang CJ, Vander Kam VM. Management of hemangioma of infancy: review of 245 patients. Plast Reconstr Surg. Apr 1997; 99(5): 1301-8.

46. Bigorre M, Van Kien AK, Valette H. Beta-blocking agent for treatment of infantile hemangioma. Plast Reconstr Surg. Jun 2009; 123(6):195e-6e.

47. Leaute-Labreze C, Dumas de la Roque E,et al. Propranolol for severe hemangiomas of infancy. N Engl J Med. Jun 12 2008; 358(24):2649-51.

48. Ezekowitz RA, Mulliken JB, Folkman J. Interferon alfa-2a therapy for life-threatening hemangiomas of infancy. N Engl J Med. May 28 1992; 326(22):1456-63.

49. Tamayo L, Ortiz DM, Orozco-Covarrubias L, et al. Therapeutic efficacy of interferon alfa-2b in infants with life-threatening giant hemangiomas. Arch Dermatol. Dec 1997; 133(12):1567-71.

50. Welsh O, Olazaran Z,et al. Treatment of infantile hemangiomas with short-term application of imiquimod 5% cream. J Am Acad Dermatol. Oct 2004; 51(4):639-42.

51. Hazen PG, Carney JF,et al. Proliferating hemangioma of infancy: successful treatment with topical 5% imiquimod cream. Pediatr Dermatol. May-Jun 2005; 22(3):254-6.

52. Boon LM, Enjolras O, Mulliken JB. Congenital hemangiomas: evidence for accelerated involution. J Pediatr 1996; 128:329-35.

53. Enjolras O, Arnaud Picard et al. Advances in Dermatology 2008; 24: 105-124.

54. Rogers M, Lam A, Fischer G. Sonographic findings in a series of RICH. Pediatr Dermatol 2002; 19:5-11.

55. Berenguer B, Mulliken JB, Enjorlas O et al. Rapidly involuting congenital hemangioma: Clinical and histopathologic features. Pediatr Dev Pathol 2003; 6:495-510.

56. Vikkula M, Boon LM, Mulliken JB, Oslen BR: Molecular basis of vascular anomalies. Trends Cardiovasc Med. 1998; 8:281.

57. Nanda A, Kaur S, Bhakoo ON et al. Survey of cutaneous lesions in Indian newborns. Pediatr Dermatol1989; 6: 39-42.

58. Merlob P, Reisner SH. Familial nevus flammeus of the forehead and Unna's nevus. Clin Genet 1985; 27: 165-6.

59. Smoller BR, Rosen S. Port-wine stains. A disease of altered neural modulation of blood vessels?. Arch Dermatol. Feb 1986; 122(2):177-9.

60. Chang CJ, Yu JS, Nelson JS. Confocal microscopy study of neurovascular distribution in facial port wine stains (capillary malformation). J Formos Med Assoc. Jul 2008; 107(7):559-66.

61. Vural E, Ramakrishnan J,et al. The expression of vascular endothelial growth factor and its receptors in port-wine stains. Otolaryngol Head Neck Surg. Oct 2008; 139(4):560-4.

62. Kaji N, Nagase T, et al. Changes in angiogenic gene expression in a case of expanded capillary malformation: does an expanded capillary malformation grow?. Ann Plast Surg. Jun 2005; 54(6):645-50.

63. Boon LM, Mulliken JB, Vikkula M. RASA1: variable phenotype with capillary and arteriovenous malformations. Curr Opin Genet Dev. Jun 2005; 15(3):265-9.

64. Finley JL, Noe JM, Arndt KA et al. Port-wine stains: morphological variations and developmental lesions. Arch Dermatol1984; 120:1453-5.

65. Tallman B, Tan OT, Morelli JG et al. Location of port wine stains and the likelihood of opthalmic and/or central nervous system complications. Pediatrics 1991; 87:323-7.

66. Happle R, Koopman R, Mier OD. Hypothesis: vascular twin naevi and somatic recombination in man. Lancet1990; 335: 376-8.

67. Kono T, Groff WF, Sakurai H. Treatment of port wine stains with the pulse dye laser. *Ann Plast Surg*. Apr 2006; 56(4):460-3.

68. Welch K, Naheedy MH, et al. Computer tomography of Sturge-Weber syndrome in infants. J Comput Assist Tomogr 1980; 4: 33-6.

69. Benedikt RA, Brown DC, Walker R et al. Sturge-Weber syndrome: cranial MR imaging with Gd-DTPA. Am J Neuroradiol 1993; 14: 409-15.

70. Hoffman HJ, Hendrick EB, Dennis M et al. Hemispherectomy for Sturge-Weber syndrome. Child's Brain 1979; 5: 233-48.

71. Baskerville PA, Ackroyd JS, Thomas ML et al. The Klippel-Trenaunay syndrome: clinical, radiological and haemodynamic features and management. Br J Surg1985; 72:232-6.

72. Young AE. Combined vascular malformations. In: Mulliken JB, Young AE, eds. Vascular Birthmarks. Philadelphia: WB Saunders 1988: 246-74.

73. Jacob AG, Driscoll DJ, Shaughnessy WJ et al. Klippel-Trenaunay syndrome: Spectrum and management. Mayo Clin Proc 1998; 73(1):28-36.

74. Viljoen DL, Saxe N, Temple-Camp C. Cutaneous manifestations of the Proteus syndrome. Pediatr Dermatol 1988; 5: 14-21.

75. Ruiz-Maldonado R, Tamayo L, Laterza AM et al. Phacomatosis pigmentovascularis: a new syndrome. Pediatr Dermatol 1987; 4: 189-96.

76. Chiller KG, Passaro D, Frieden IJ. Haemangiomas of infancy. Clinical characteristics, morphologic subtypes and their relationship to race, ethnicity and sex. Arch Dermatol 2002; 138:1567-76.

77. Senthilkumar M, Thappa DM. Vascular nevi in children. Indian J Dermatol Venereol Leprol 2006; 72:19-23.

78. Bruckner AL, Frieden IJ. Hemangiomas of infancy. J Am Acad Dermatol 2003; 48:477-93.

79. Finn MC, Glowaski J, Mulliken JB. Congenital vascular lesions: clinical application of a new classification. J Pediatr Surg 1983; 18:894-9.

80. Tallman B, Tan OT,et al. Location of port-wine stains and the likelihood of ophthalmic and/or central nervous system complications.J Am Acad Pediatrics. 1991 Mar; 87(3):323-7.

81. Juliette M.H, Samira Syed, John I. Harper. Bilateral Facial Capillary Malformation Associated With Eye and Brain Abnormalities. Arch Dermatol. 2006; 142:994-99.

82. Bioxeda P, de Misa RF, Facial angioma and the Sturge-Weber syndrome**:**Med Clin (Barc). 1993 May 29; 101(1):18-9.

PROFORMA

SI. No : Case No. :

Name : Age :

Sex :

Informant : Address :

Complaints :

History of presenting illness:

Skin lesion :

Site :

Age of onset :

Mode of evolution :

Sudden increase in size / Regression of lesion (spontaneously or with treatment)

Bleeding on trauma/ Ulceration over lesion

Pain/ Recurrent infection

Sudden change in colour of lesion

Difficulty in breathing/ feeding difficulty

Hearing difficulty / Speech difficulty/ Visual disturbance

Headache, seizures

Haematuria, malena, haematemesis

Gait disturbance

Bladder disturbance

History of past illness:

Bleeding diathesis

Family history:

Similar lesions among family members

Antenatal history/ Natal history:

Alcohol intake

Any intervention (chorionic villi sampling)

Prematurity / LBW

Oxygen therapy

Developmental history:

Any delay in developmental mile stone

Treatment history:

Medical/ Surgery/ Laser

General Examination:

Build/ Appearance

Anemia/ Jaundice/ Cyanosis

Gait /Limb length/ Limb girth

Cardiac/ Respiratory status

Dermatological Examination

Site:

No. of lesion: single/multiple

No. of dermatome involved:

Unilateral/ Bilateral

Morphology: macule/papule/plaque

Lesion subtype: localized/ segmental/ indeterminate/ multifocal

Surface/ Skin changes over lesion: any ulceration, bleeding

Varicose veins (if any)

Palpation:

Warmth

Consistency

Compressibility

Mucosal involvement:

Investigation:

Haemogram

Bleeding time

Clotting time

Platelet count

Hb%, TC, DC, ESR

X-RAY chest

Radiological (Individualised as per requirements in each case)

X-RAY soft tissue of affected region

USG abdomen

Doppler

CT &MRI

Ophthalmological examination in relevant cases

Biopsy (in selected cases)

Diagnosis :

Follow up : 6 months 1year 1.5years 2years

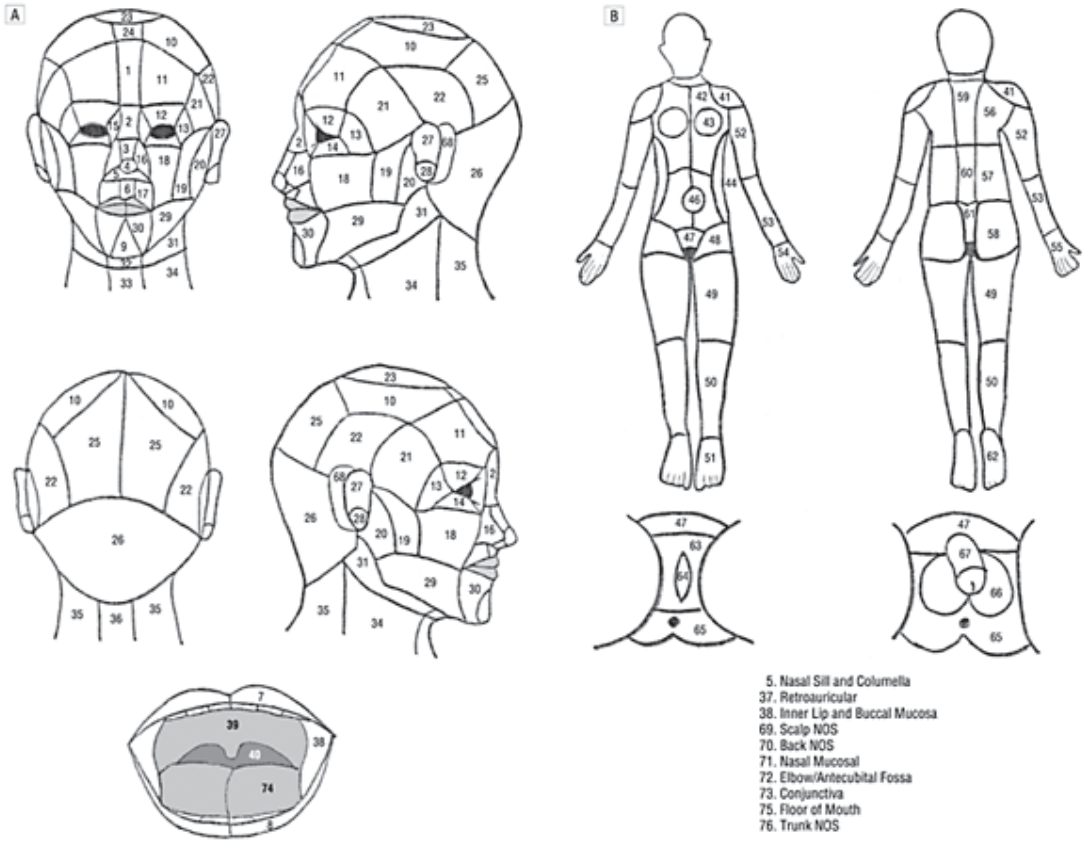

A
B
5. Nasal Sill and Columella
37. Retroauricular
38. Inner Lip and Buccal Mucosa
69. Scalp NOS
70. Back NOS
71. Nasal Mucosal
72. Elbow/Antecubital Fossa
73. Conjunctiva
75. Floor of Mouth
76. Trunk NOS

Figure 15

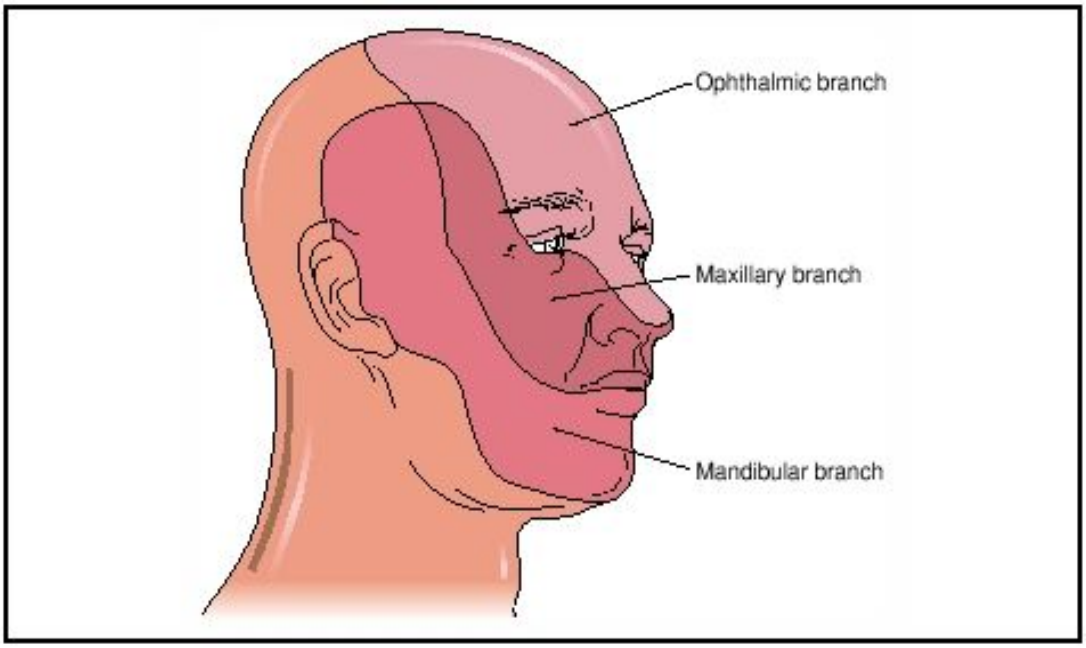


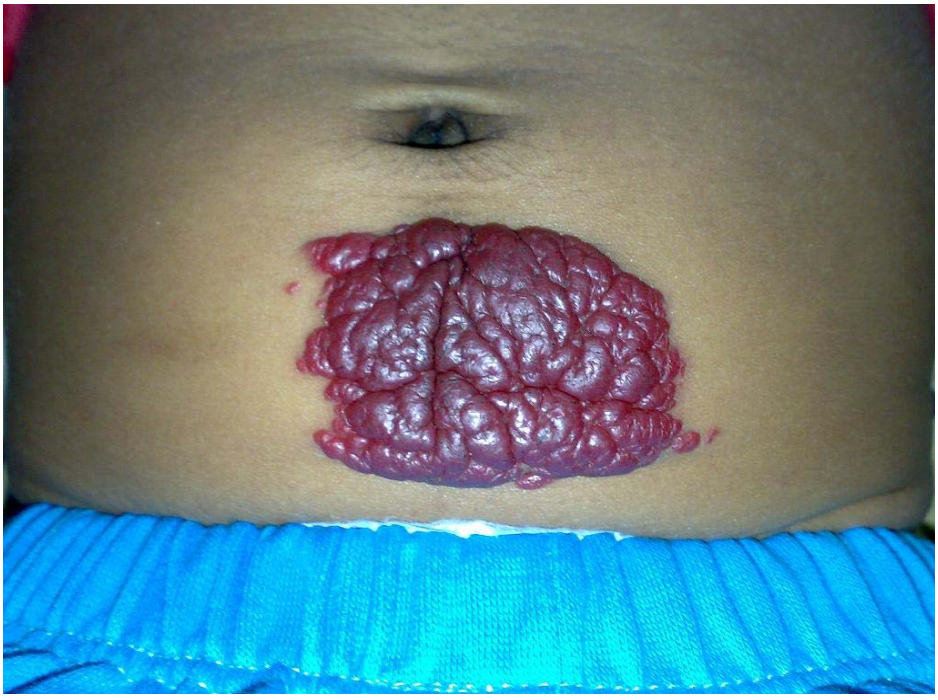
Figure 16

Hemangioma below right eye

Hemangioma over the scalp

Hemangioma involving the chest

Hemangioma over the abdomen

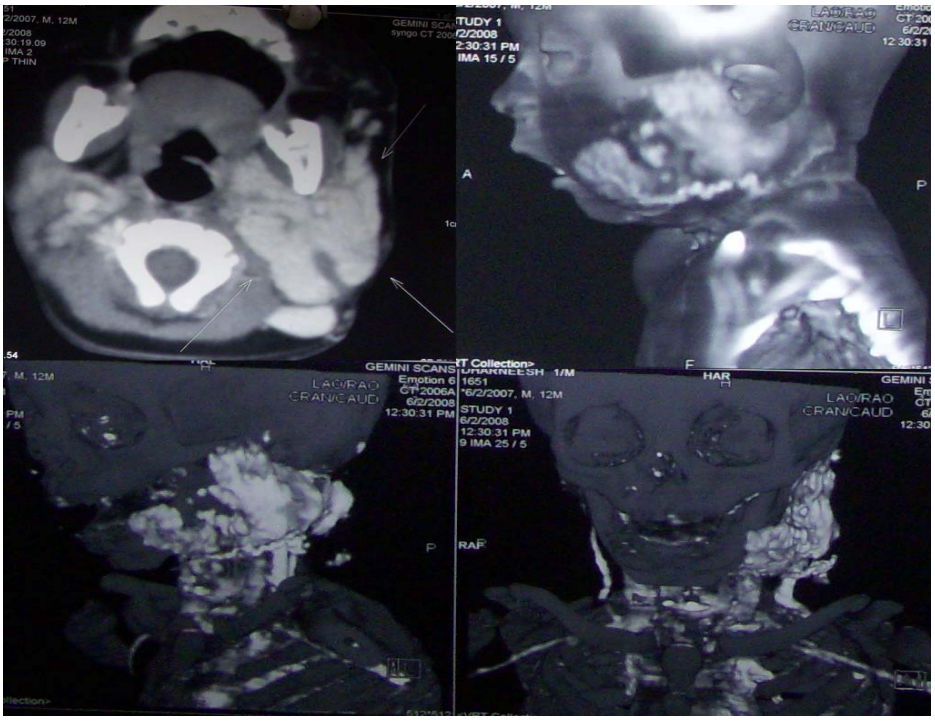


Segmental hemangioma of right forearm

Hemangioma involving the back

Hemangioma of left cheek

MRI showing subglottic involvement



Hemangioma of left shoulder

Hemangioma of left shoulder (Regressing)

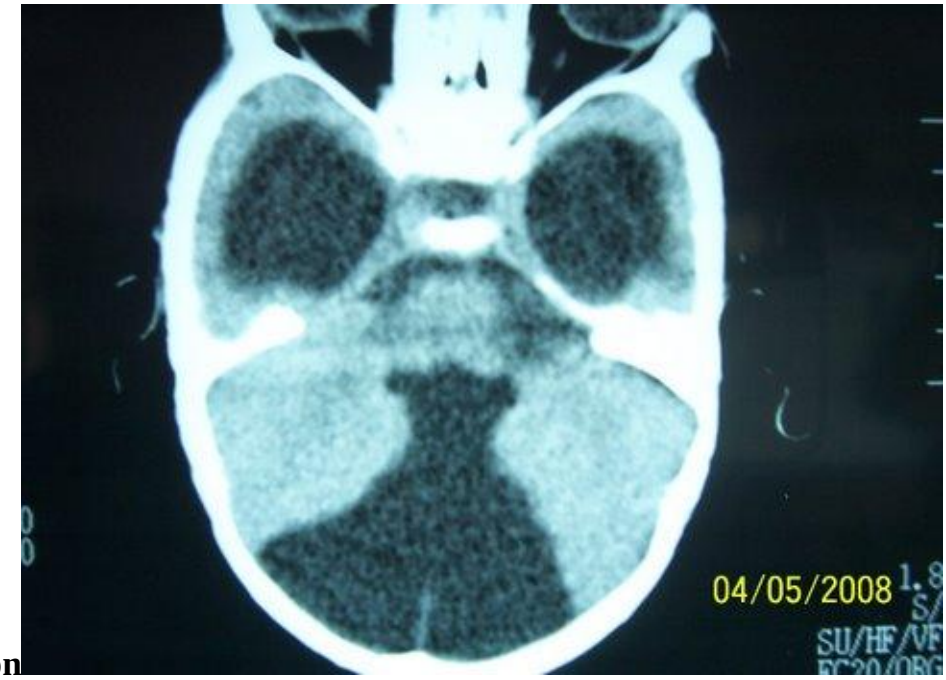
Hemangioma over left arm with ulceration

Hemangioma of genitalia with ulceration

Mucosal involvement

Hemangioma of left side of face with hydrocephalus and occlusion of eye

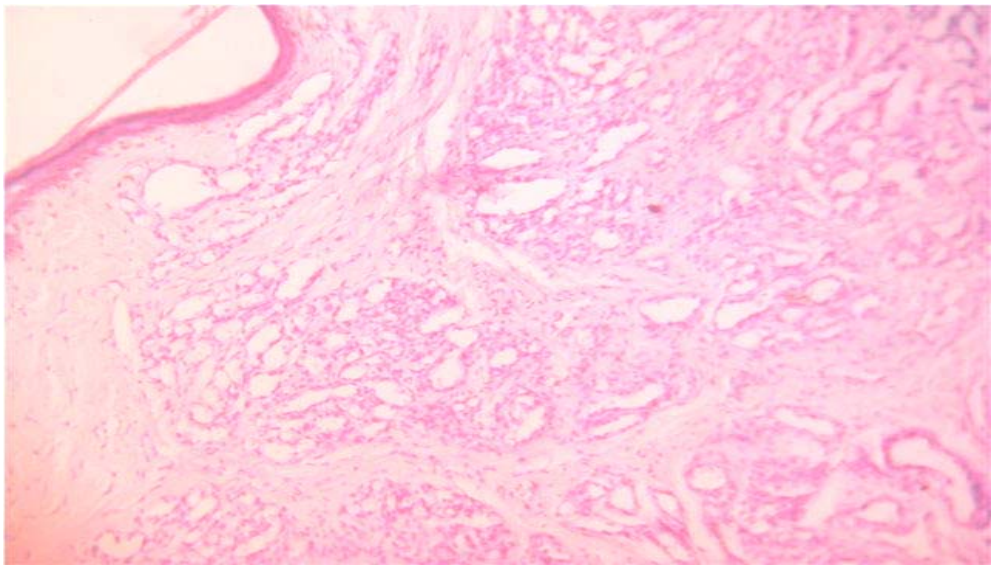
CT scan showing Dandy Walker malformation

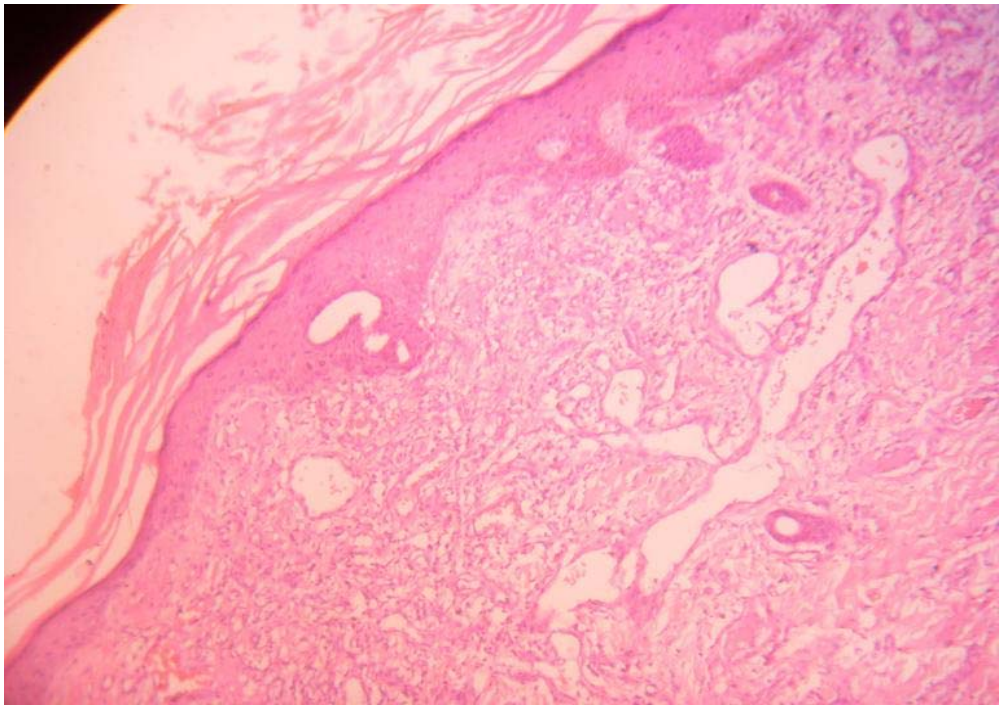


Segmental hemangioma of face with ulceration, breathing and feeding difficulty

Multifocal hemangioma

Histopathology of hemangioma showing multiple vascular spaces lined by endothelial cells



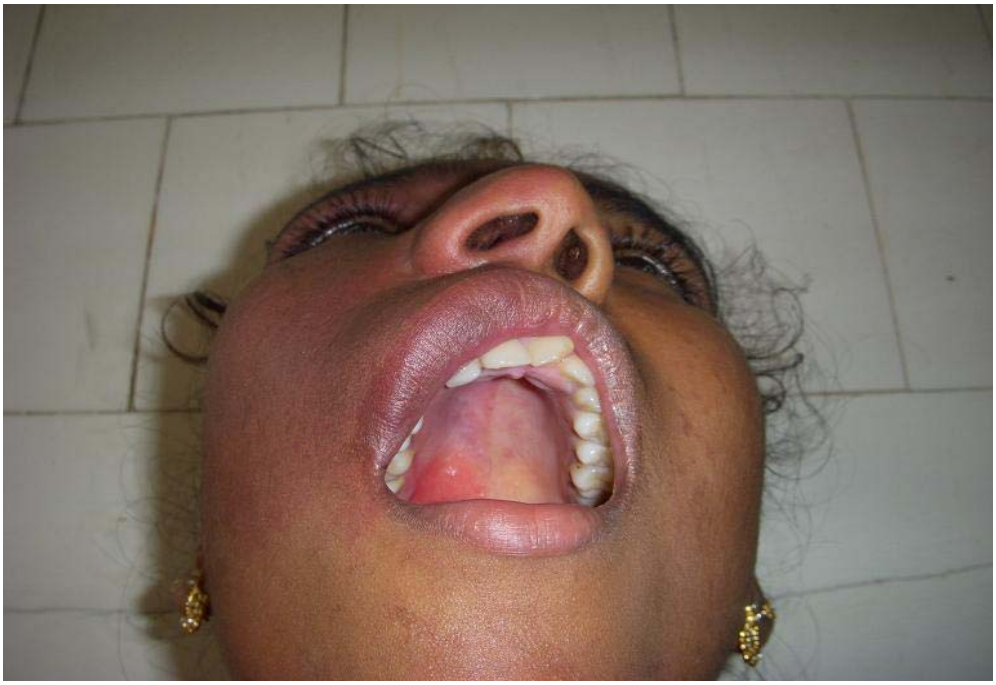


Hemangioma over Left leg (showing bleeding)

After excision

Unilateral portwine stain with involvement of both upper and lower eyelid

Mucosal involvement



Bilateral portwine stain with nevus of ota of left side

Mucosal involvement

Bilateral portwine stain with congenital melanocytic naevi

Unilateral portwine stain with sparing of upper eyelid

Portwine stain of right side of face

Linear epidermal naevi involving right arm and forearm

Cases of Klippel Trenaunay syndrome showing portwine stain, venous varicosity and limb hypertrophy

MASTER CHART - VASCULAR MALFORMATIONS

Case no	Age	Age of onset	Gender	No of derm.inv	Site of lesions	Mucosal involvement	Uni/Bilateral	Trigeminal br.	Complications	CBC	Other Investigations	Associations
1	42Y	Birth	F	Multiple	Face	Yes	Unilateral	Max	-	Normal	CT-N	-
2	6Y	Birth	F	Multiple	Face	No	Unilateral	Max,oph	-	Normal	CT-N	-
3	18Y	Birth	F	Multiple	Leg	-	-	-	Gait disturbance	Normal	Doppler,X-Ray	Ven Var& LH
4	35Y	Birth	M	Single	Face	No	Unilateral	Max	-	Normal	-	-
5	32Y	Birth	F	Multiple	Face	No	Unilateral	Max		Normal	CT-N	-
6	20 Y	Birth	M	Multiple	Leg	-	-	-	Gait disturbance	Normal	Doppler,X-Ray	Ven Var& LH
7	37Y	Birth	M	Single	Face	No	Unilateral	Max	-	Normal	-	-
8	25Y	Birth	M	Single	Face	No	Unilateral	Oph	-	Normal	-	-
9	19Y	Birth	F	Multiple	Face	Yes	Bilateral	Oph,Max,Man	Seizures&Glaucoma	Normal	CT-N	CMN
10	60Y	Birth	F	Multiple	Face	Yes	Unilateral	Max	Glaucoma	Normal	CT-N	-
11	15Y	Birth	F	Multiple	Face	Yes	Unilateral	Oph,Max,Man	Seizures	Normal	CT-N	-
12	25Y	Birth	M	Single	Face	No	Unilateral	Max	-	Normal	CT-N	-
13	1Y	Birth	M	Multiple	Face	No	Unilateral	Max	-	Normal	-	Linear Epi Nevi
14	20Y	Birth	F	Multiple	Face	Yes	Bilateral	Oph,Max,Man	Glaucoma	Normal	CT-N,MRI	Nevus of ota, CMN
15	62Y	Birth	M	Multiple	Hand	-	-	-	-	Normal	-	-

MASTER CHART - VASCULAR MAL FORMATIONS

Case no	Age	Age of onset	Gender	No of derm.inv	Site of lesions	Mucosal involvement	Uni/Bilateral	Trigeminal br.	Complications	CBC	Other Investigations	Associations
16	40Y	Birth	M	Single		-	-	-	-	Normal	-	-
17	20Y	Birth	F	Single	Back	-	-	-	-	Normal	-	-
18	36Y	Birth	F	Single	Face	No	Unilateral	Oph	-	Normal	-	-
19	45Y	Birth	M	Multiple	Face	No	Unilateral	Max	-	Normal	CT-N	-
20	20Y	Birth	F	Multiple	Face	Yes	Bilateral	Oph,Max,Man	Seizures	Normal	MRI	Pitu MA

MON = Month
F = Female
M = Male
Prog = Progressive
Reg = Regressive
Non-inv = Non-involuting
N = Normal
Oph = Ophthalmic
Indeter = Indeterminate

Fd = Feeding difficulty
Bth = Breathing difficulty
CMN = Congenital melanocytic nevi
Ven Var = Venous Varicosity
LH = Limb Hypertrophy
Pitu MA = Pituitary Microadenoma
Max = Maxillary
Man = Mandibular

MASTER CHART - HEMANGIOMAS

Case no.	Age	Age of Onset	Gender	Family History	Term/ Pre-term	Birth weight	No. of lesions	Lesion subtype	Distribution of lesions	Course	Complication	Mucosal inv	CBC	Other investigations	Associations
1	9MON	Birth	F	No	Term	2.8 Kg	Single	Localised	Face	Reg	Nil	No	N	MRI-Normal	-
2	8MON	1MON	F	No	Term	3 Kg	Single	Localised	Back	Prog	Nil	No	N	-	-
3	3MON	Birth	F	No	Term	2.9 Kg	Single	Localised	Back	Prog	Nil	No	N	-	-
4	1Y	Birth	F	No	Term	2.6 Kg	Single	Localised	Chest	Reg	Nil	No	N	-	-
5	2Y	Birth	F	No	Term	3 Kg	Single	Localised	Face	Non-inv	Nil	No	N	CT-Normal	-
6	6Y	3MON	F	Yes	Term	3.25 Kg	Multiple	Indeter	Leg	Non-inv	Bleeding	No	N	X-RAY-N/Biopsy	-
7	4Y	2MON	M	No	35 Weeks	1.8 Kg	Single	Localised	Leg	Non-inv	Nil	No	N	X-RAY-N	-
8	2MON	Birth	F	No	Term	2.75 Kg	Single	Localised	Face	Non-inv	Nil	No	N	-	-
9	2MON	Birth	F	No	Term	2.6 Kg	Single	Segmental	Hand	Prog	Nil	No	N	-	-
10	4MON	Birth	F	No	Term	3.3 Kg	Single	Localised	Scalp	Non-inv	Nil	No	N	CT-Normal	-
11	5MON	Birth	F	No	Term	2.9 Kg	Single	Indeter	Hand	Prog	Nil	No	N	-	-
12	1MON	Birth	M	No	Term	2.75 Kg	Single	Localised	Back	Prog	Nil	No	N	-	-
13	7Y	Birth	F	No	Term	3 Kg	Single	Segmental	Face	Reg	Nil	Yes	N	CT-Normal	-
14	4MON	Birth	M	No	31 Weeks	1.3 Kg	Single	Segmental	Face	Non-inv	Fd/Bth	Yes	N	MRI-Subglottic inv	Subglottic inv
15	3MON	Birth	F	No	Term	2.8 Kg	Single	Localised	Hand	Non-inv	Nil	No	N	-	-

MASTER CHART - HEMANGIOMAS

Case no.	Age	Age of Onset	Gender	Family History	Term/ Pre-term	Birth weight	No. of lesions	Lesion subtype	Distribution of lesions	Course	Complication	Mucosal inv	CBC	Other investigations	Associations
16	5MON	Birth	F	No	Term	3.2 Kg	Single	Localised	Scalp	Non-inv	Nil	No	N	-	-
17	15D	Birth	F	No	Term	2.7 Kg	Multiple	Indeter	Back	Prog	Nil	No	N	-	-
18	1.2Y	1MON	F	No	Term	3.1 Kg	Single	Localised	Face	Non-inv	Nil	No	N	-	-
19	1.8Y	1MON	M	No	Term	2.6 Kg	Single	Localised	Scalp	Non-inv	Nil	No	N	-	-
20	1.5Y	Birth	F	No	34 Weeks	2.25 Kg	Single	Localised	Scalp	Non-inv	Ulceration	No	N	-	-
21	2Y	Birth	F	No	Term	3 Kg	Single	Localised	Hand	Non-inv	Ulceration	No	N	X-RAY-N/Biopsy	-
22	1MON	Birth	M	Yes	35 weeks	2.6 Kg	Single	Segmental	P	Prog	Vision	No	N	CT-Dandy Walker/Echo	Hydrocephalus
23	1.5Y	1MON	F	No	Term	3.1 Kg	Single	Localised	Genital	Non-inv	Ulceration	Yes	N	-	-
24	3Y	Birth	M	No	34 weeks	2 .25Kg	Single	Indeter	Hand	Non-inv	Bleeding	No	N	Biopsy	-
25	4Y	Birth	M	No	Term	2.9 Kg	Single	Localised	Hand	Reg	Nil	No	N	-	-
26	2MON	Birth	F	No	32 Weeks	2 Kg	Multiple	Segmental	Face	Prog	Fd/Bth/Ulceration	Yes	N	CT-Normal	-
27	4MON	Birth	M	No	Term	3.2 Kg	Single	Localised	Chest	Prog	Nil	No	N	-	-
28	1.5Y	Birth	F	No	36 Weeks	2.75 Kg	Single	Localised	Abdomen	Non-inv	Ulceration	No	N	-	-
29	2Y	Birth	F	Yes	Term	2.8 Kg	Single	Localised	Hand	Non-inv	Nil	No	N	-	-
30	2MON	Birth	F	No	Term	2.6 Kg	Multiple	Multifocal	Multiple	Prog	Nil	No	N	USG abdomen-N	-

MASTER CHART - HEMANGIOMAS

Case no.	Age	Age of Onset	Gender	Family History	Term/ Pre-term	Birth weight	No. of lesions	Lesion subtype	Distribution of lesions	Course	Complication	Mucosal inv	CBC	Other investigations	Associations
31	5Y	Birth	F	No	Term	3.1 Kg	Single	Localised	Abdomen	Non-inv	Nil	No	N	-	-
32	1MON	Birth	F	No	Term	2.75 Kg	Single	Indeter	Abdomen	Non-inv	Ulceration	No	N	-	-
33	5MON	Birth	F	No	Term	3 Kg	Single	Localised	Scalp	Non-inv	Nil	No	N	-	-
34	3MON	Birth	F	Yes	Term	3 Kg	Single	Localised	Face	Prog	Nil	No	N	-	-
35	2MON	Birth	F	No	Term	2.7 Kg	Single	Localised	Face	Non-inv	Nil	No	N	-	-
36	1.4Y	Birth	F	No	Term	3.25 Kg	Single	Indeter	Scalp	Non-inv	Bleeding	No	N	-	-